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RESPIRATORY FAILURE IN POLIOMYELITIS

TREATMENT WITH THE DRINKER RESPIRATOR

JAMES L. WILSON, M.D.

BOSTON

Of all the experiences that the physician must undergo, none can be more distressing than to watch respiratory paralysis in a child ill with poliomyelitis—to watch him as he becomes more and more dyspneic, using with increasing vigor every available accessory muscle of neck, shoulder and chin, silent, wasting no breath for speech, wide-eyed and frightened, conscious almost to the last breath. When Professor Drinker first developed his machine for artificial respiration to a practical point in 1928, the staff of the hospital, of course, were more than willing to give him an opportunity to use it on such a child. His experience with that child was reported at the time.[1]

The Drinker respirator has now frequently been described, and the results of its action on numerous patients reported.[2] Briefly, it consists of an air-tight metal chamber in which a patient can be conveniently placed so that the head protrudes through a flat, soft, rubber collar, which is attached to the front of the machine, and which fits comfortably

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around the neck. The patient's body, excepting the head, is completely enclosed within the machine. With a suitable suction pump and alternating valve arrangement, the pressure inside the chamber is rhythmically varied between atmospheric pressure and a partial vacuum. The pressure changes in turn act on the thorax and abdomen of the patient but not on the nose and throat. The degree of pressure change and the rate of alternation can be varied at will. The net effect is that respiration is induced in a manner which seems to simulate normal respiration fairly accurately. The machine that we used most frequently could be tilted to allow postural drainage and could be rotated on its long axis so that the patient could lie on his side.

Since 1928, we have observed the response to the action of the respirator of seventeen patients with poliomyelitis, who have suffered from respiratory failure either because of paralysis of the diaphragm and intercostal muscles or from involvement of the bulbar nerves and presumably also the respiratory centers.

The conclusions in this report are drawn from clinical and pathologic observations. We have attempted to correlate these data with physiologic studies, but measurements of the vital capacity or of the alveolar carbon dioxide of these easily frightened children have been, so far, unsuccessful in our hands. Although the patients were resting comfortably in the machine, without dyspnea, any attempt to fasten paraphernalia over their faces during the acute phase of the illness met with such evidence of fear and distress that it was impossible to secure reliable measurements. Because of the construction of the respirator, samples of blood for chemical analysis are most difficult to obtain. In order to carry out such studies, we have now, however, in process of manufacture, a modification of the respirator that will enable us to do venipunctures without stopping the machine.

PROBLEMS OF THERAPY

In the application of this form of treatment a number of problems of a practical nature have arisen, the solution of which we have attempted to determine. The more important questions are: 1. In what types of respiratory failure in poliomyelitis is the use of the respirator indicated? 2. Is the use of the respirator attended with harmful effects, either (*a*) on the structure of the lungs themselves, or (*b*) by disturbing the acid-base equilibrium of the body? 3. If a patient with intercostal and diaphragmatic paralysis due to poliomyelitis can be kept alive by artificial respiration during the acute stage, will the involved muscles ultimately regain power to an extent enabling him to breathe alone? 4. At what stage of the disease is the use of the machine indicated?

1. *In what types of respiratory failure is the use of the respirator indicated?*

The patients in this series of cases with respiratory difficulty have fallen rather sharply into two groups: (*a*) those with simple paralysis of the intercostal muscles, of the diaphragm, or of both together and (*b*) those with involvement of the bulbar nerves and presumably the respiratory centers.

(*a*) Exact determination of the extent of the paralysis of the intercostal muscles or of the diaphragm is important. Usually the paralysis of the intercostal muscles and of the diaphragm is partial and coexistent, and in a child who will not cooperate by "taking a deep breath" the determination of the relative extent of the weakness of the two groups of respiratory muscles is difficult. If the abdominal wall is splinted with the hands, the action of the diaphragm can be inhibited, and a resulting dyspnea may strikingly demonstrate a paralysis of the intercostal muscles. In a similar manner, the thorax can be splinted with the hands and the efficiency of the action of the diaphragm studied.

With complete paralysis of the diaphragm, without associated involvement of the intercostal muscles, there is present a noticeably excessive motion of the thorax, and it can be observed that the abdominal wall moves inward on inspiration instead of outward as is normal. Extensive paralysis of the intercostal muscles not associated with diaphragmatic weakness can be present without causing such striking signs. The diaphragm is quite capable of maintaining normal respiration for some time, alone, and a moderate indrawing of the thoracic walls along the line of attachment of the diaphragm may be the only evidence of intercostal weakness.

Of this first group, we have had experience with six patients (cases 1 to 6). The relief obtained with the use of the respirator by each of these six children with intercostal and diaphragmatic weakness was almost invariably immediate and striking. Within a minute after the child was placed in the respirator, there was complete synchronism of the respiratory efforts of the patient with the rhythm of the machine, almost complete cessation of evidences of dyspnea, and usually sleep. The children in this group stayed in the machine for varying periods of from one to six weeks. The action of the machine in maintaining prolonged artificial respiration and in aiding patients with a reduced vital capacity was entirely satisfactory.

(*b*) The second group of children with acute poliomyelitis and respiratory failure must be sharply distinguished from the simple type with paralysis of the intercostal muscles or of the diaphragm that I have just described, although both conditions may exist together (case 6). We have had experience with eleven children (cases 7 to 17)

this past season with the bulbar type of infantile paralysis, who have had no paralysis of the intercostal muscles or of the diaphragm, but who have had nevertheless such disturbances of respiration that we have attempted to aid them by the use of the respirator. All of these children had definite involvement of the muscles of deglutition, and some of them showed involvement of other bulbar nerves. The disturbances of respiration were apparently due to involvement of the "centers" of respiratory control in the medulla. None of this group showed clinical evidences of cortical irritation as manifested by convulsions. The type of the disease which these patients manifested is commonly included in the group described as "bulbar" poliomyelitis—a term that I will use.

In the children of this group, fever, headache, vomiting and signs of meningeal irritation characterized the preparalytic stage, which, except perhaps for the unusually persistent vomiting, did not vary consistently from the first stages of the "spinal" type of poliomyelitis. On the second to fourth day, the first signs of pharyngeal paralysis appeared. Most frequently it made itself first evident by a choking attack, initiated by vomiting, but it was sometimes preceded for a short interval by a nasal voice and regurgitation through the nose. Again, mucus in the throat may produce an ominous gurgling respiration, which, occurring in an alert conscious child, may first attract the physician's attention. In several cases the examiner himself first demonstrated to the patient his disability in a distressing way, by offering a drink of water. The child may take the water eagerly only to exhibit a look of intense surprise and fear as he throws himself over the side of the bed in an attack of coughing and choking. Many such patients become no worse. Nursing care, aspiration of the throat, postural drainage for a relatively few days, may help them during the acute febrile stage, and recovery is then prompt and usually complete. In eleven patients (cases 7 to 17) with the bulbar type of poliomyelitis, however, the disease progressed to a much more critical situation. In these children the choking attacks, usually associated with vomiting, became more frequent; cyanosis was evident not only during an attack of choking but continuously. Frequently such an attack of choking and cyanosis was followed by a definite change for the worse in the patient's condition. The children became semiconscious, and the respirations became shallow, irregular, and so obviously inefficient that we attempted to give what aid we could by the use of the respirator.

It is much more difficult to evaluate the use of the respirator in the patients with bulbar involvement than in those with simple paralysis of the intercostal muscles or the diaphragm. In the beginning of our study of the use of the respirator, we considered its application limited exclusively to the latter forms of paralysis. Two children, cases 7 and 8, however, admitted in quick succession, aroused our interest in further

possibilities of the machine. These boys had paralysis only of the muscles of deglutition, and when first seen, no evidence of involvement of respiration. There were frequent attacks of vomiting and choking. In both these children, following one such attack, respirations ceased. Postural drainage, aspiration of the throat, as well as artificial respiration by the manual method were all without apparent aid. After a few minutes, the heart still beating, the children were placed in respirators which were tilted to permit drainage. Air passed in and out of the lungs immediately—cyanosis diminished and very soon the children began to make spontaneous attempts at respiration. After short intervals, as their ability to breath effectively had apparently returned, they were removed from the respirators, but because of cyanosis and recurring irregular breathing were both put in machines a second time with again apparently definite aid. Both these children recovered completely. The exact mechanism of this sudden collapse of respiration is not clear to us.

The other nine patients with bulbar involvement (cases 9 to 17) were somewhat different from these two boys. Sudden complete cessation of respiration did not take place, but there was rather a progressive loss of consciousness with increasing irregularity of respiration which became more and more inefficient with resulting deepening cyanosis.

Seven of these nine patients died (cases 11 through 17). The course of their illness was for the most part short, characterized by irregular, jerky, interrupted respirations, cyanosis and an increasingly marked tachycardia.

The action of the heart in these patients deserves further mention. The rate was frequently around 200, and the pulse was often very difficult to palpate because of its rapidity and its poor tone. Each of the seven children who died exhibited this extreme tachycardia for some hours before death. Although a tachycardia of considerable magnitude occurred in some of the patients in this series who survived, we consider a gradually increasing heart rate to be a most ominous sign. We were unable to obtain any apparent aid from the use of the digitalis series in these cases.

When the use of the respirator on the patients with a disturbed central control of respiration was attempted, there was for much of the time a lack of synchronism between their respiratory efforts and the rhythm of the machine. This reaction to the respirator is of greatest importance in judging the effectiveness of the machine on a patient. If the patient attempts inspiration during the expiratory phase of the respirator or, as is more striking, obstructs the ingress of air by apparently closing the glottis during the inspiratory phase, it is obvious that the machine can give no aid. An apparent reflex closure of the upper air passages during the inspiratory phase of the

respirator was very frequent in this group of patients. We are not sure whether this reaction is entirely due to a disturbance of the respiratory centers as such or whether a reflex spasm of the larynx due to a local irritation from unswallowed mucus is an important factor. The children were tilted at as sharp an angle as was possible in an effort to aid drainage. At times definite aid seemed to be obtained by the use of morphine in an attempt to so depress the respiratory centers that the action of the respirator would be unopposed by the patient's own spasmodic and ineffective respiratory efforts. This measure, radical as it seems, was apparently of considerable aid in two children (cases 9 and 10) with irregular breathing, who survived. As far as one could judge by simple observation, the survival of these two children seemed to a large extent due to their favorable response to the action of the respirator, although in the period just before they were placed in the machine, when their condition seemed most desperate, there was nothing that we observed which enabled us to offer a better prognosis to them, than to those who died.

In certain cases we have found it difficult to distinguish between respiratory disturbances due to paralysis of the intercostal muscles and apparent damage to the respiratory centers.

In the eleven children of this group (with purely bulbar involvement), paralysis of the intercostal muscles was frequently, for short periods, thought to be present. The irregular and inefficient breathing, often shallow and often combined with the use of the accessory muscle of respiration in the neck, was confusing. The subsequent course of the disease showed that this paralysis had not occurred.

In one child (case 2) we at first thought that we were dealing with only an involvement of the respiratory centers. He breathed very irregularly, and we could detect no intercostal or diaphragmatic weakness. He did not, however, have paralysis of any bulbar nerves. He responded immediately to the use of the respirator, showing immediate and complete relief from dyspnea. Later we found both shoulders paralyzed and a very definite paralysis of the intercostal muscles.

Only one of the patients had actual involvement of bulbar nerves as well as paralysis of intercostal muscles (case 6).

The answer to the first question "In what types of respiratory failure is the use of the respirator indicated?" can in our experience, thus be summarized: The Drinker respirator seemed ideally efficient in patients with poliomyelitis who have paralysis of the intercostal muscles or of the diaphragm. It seemed very effective in two children with bulbar involvement who had sudden complete cessation of respiration. It was usually inefficient and often entirely ineffective when there existed a disturbed central control of the rhythm of respiration. We were not

always able to estimate the possible aid to be obtained from the respirator before actual clinical trial.

2. *Does the machine do harm either (a) to the structure of the lung or (b) by disturbance of the acid-base equilibrium of the body?*

(*a*) All of the children with paralysis of the respiratory muscles lived. In one there was clinical evidence of a possible rupture of alveoli of the lung. During the treatment of this child (case 2), because of a defect in the manometer by which the pressure in the tank is determined, the machine was inadvertently run at high pressure for several hours. The exact pressure given is not known. The child slept during this period and showed no indications of distress, but the next day a moderate amount of subcutaneous emphysema appeared on the left side of his neck, which gradually disappeared over a course of several days. The boy had severe bronchitis, and we were not sure that the emphysema resulted from excessive ventilation due to the respirator, or was one of the complications occasionally seen with certain types of respiratory infection.

Necropsies were performed on three of the children in this series (cases 11, 16 and 17), and so the opportunity was provided to study the changes in the lungs in patients who had been treated in the respirator. The three patients had bulbar involvement, without evidence of paralysis of the intercostal muscles or of the diaphragm. Each patient died in the respirator with evidences of cardiac failure. The pathologic changes in each instance were so similar as to make it unnecessary to discuss them separately.

The central nervous system showed lesions of the medulla characteristic of poliomyelitis. Histologic study of the medulla revealed no sharply localized lesions that would explain individual clinical symptoms. The vagus nucleus was involved, but no more than other portions of the brain stem. No demonstrable lesions of the heart were found to explain the sudden failure. The lungs were of great interest, and we find it difficult wholly to evaluate our observations, which were somewhat similar to those recently reported by Murphy, Drinker and Drinker in adults.[3]

Grossly, the lungs showed emphysema of the anterior portions and varying amounts of congestion, bronchopneumonia and hemorrhagic areas in the dependent parts. In one case (11) bronchopneumonia was very extensive.

Histologically, there was marked congestion of all the blood vessels, transudation of serum and red blood corpuscles into the alveolar spaces and, in sections from the anterior parts of the lung, emphysema. The emphysema was sometimes marked, with large air spaces, occasionally

3. Murphy, Drinker and Drinker (footnote 2).

the extent of an entire low power field. In some areas a narrow rim of serum precipitate and red blood corpuscles was seen apparently compressed against the sides of the alveolar walls by air bubbles. It was to be noted that the amount of serum and red blood cells was much greater than was consistent with the amount of evident inflammatory reaction. It is also noteworthy that the amount of serum exudate and

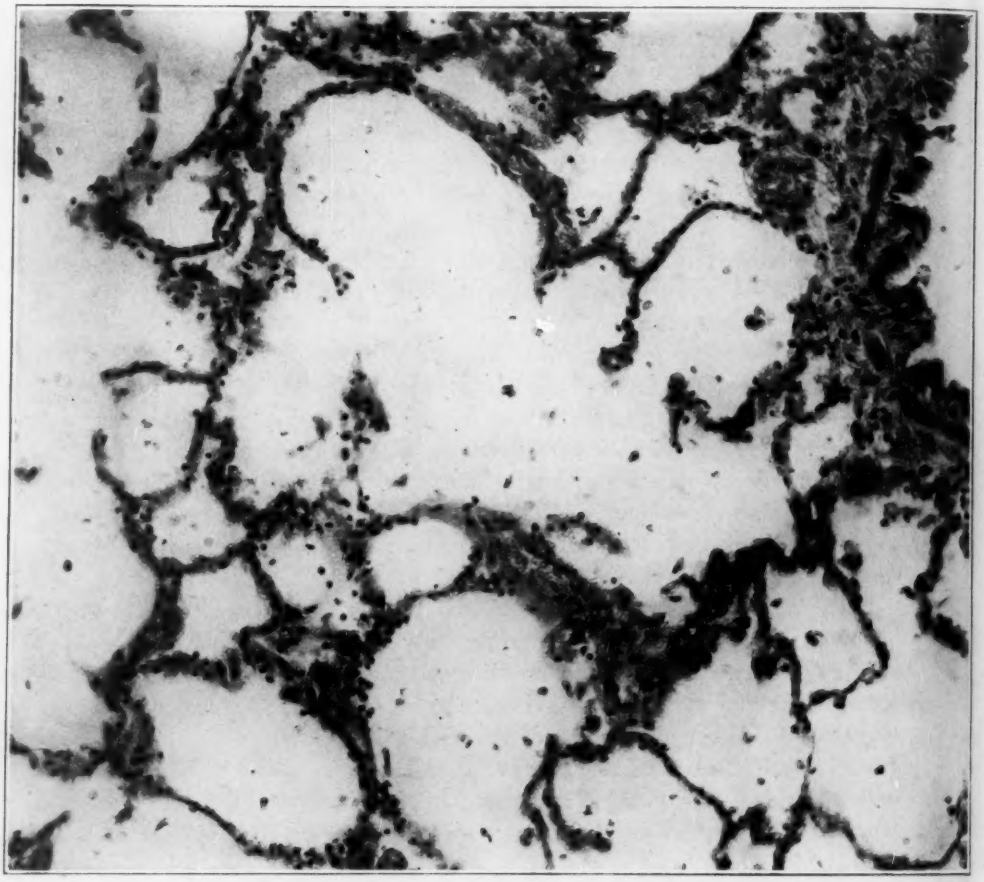

Fig. 1 (case 11).—Low power photomicrograph (hematoxylin and eosin stain) from the anterior part of the lung, showing dilated alveoli in the emphysematous area. Note the thinned alveolar walls.

the extent of capillary engorgement was much greater in the dependent portion of the lungs than in the anterior emphysematous areas where often the alveolar walls seemed pressed out and thin.

A large amount of the serum transudate and of the emphysema we attribute to the use of the respirator. However, it was interesting

in reviewing the slides of similar cases of past years when the machine had not been used, to discover in these children likewise, similar emphysema and congestion, though of a considerably less degree.

From our pathologic observations then we have evidence that the respirator may have done harm. We feel, however, first, that the patient himself, had he the strength to do so, might well have brought

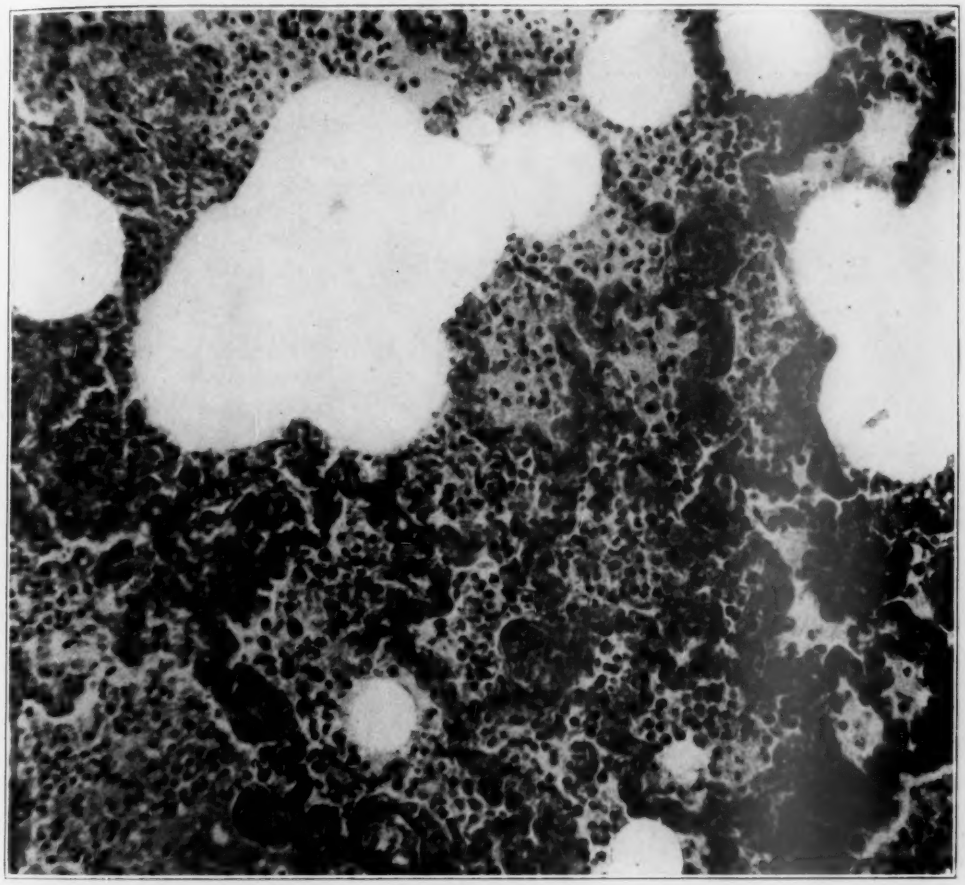

Fig. 2 (case 16).—Low power photomicrograph (hematoxylin and eosin stain) of a section from the dependent portion of the lung. The alveoli is distended with air in a zone of pneumonic infiltration. Marked congestion and distention of the vessels in the alveolar walls is shown.

about similar changes in the lungs in his last efforts to maintain life; second, that much of the damage may be due to an excessive use of the respirator just before and immediately after death. It is, of course, to be remembered that each child was subjected to vigorous artificial

respiration immediately before and for varying periods after death. The exact moment of death was often difficult to determine, and there was a natural tendency, quite justifiable, to increase the power of the machine in a final effort to prolong life. After death, the glottis apparently relaxes so that the protective spasm of the larynx no longer prevents excessive pulmonary distention.

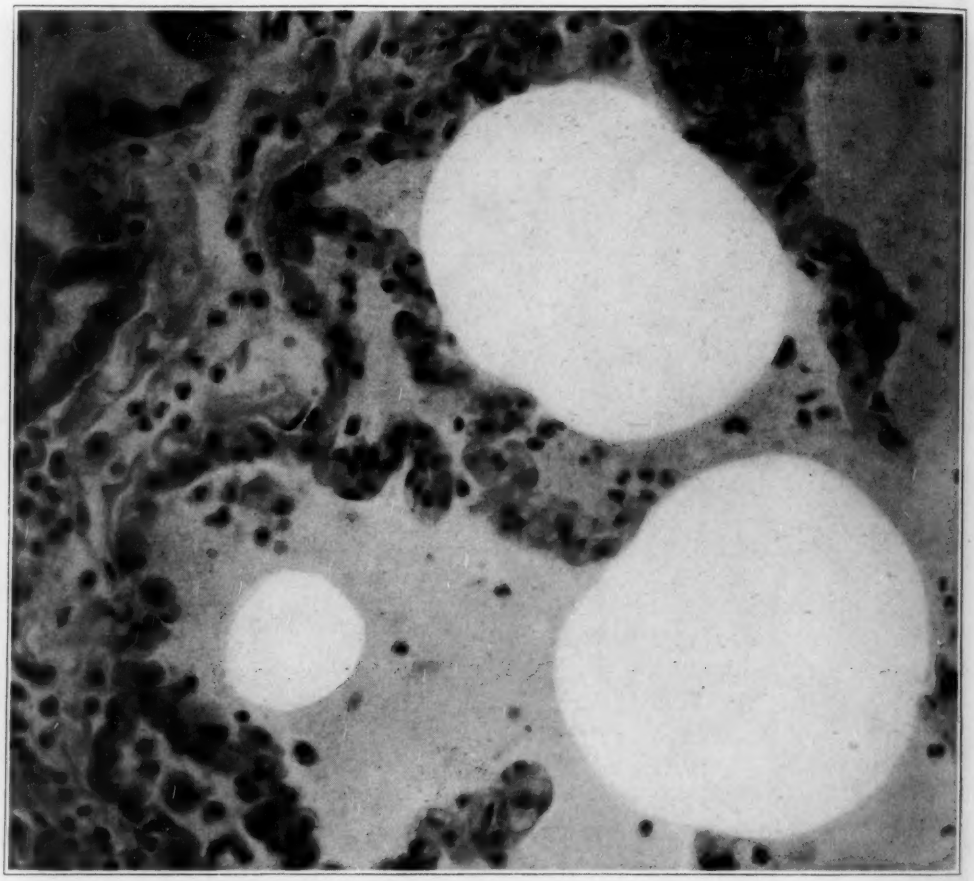

Fig. 3 (case 16).—High power photomicrograph of a section of the lung from a dependent portion (hematoxylin and eosin stain). The dilated alveoli contains large amounts of serous precipitation surrounding areas of air. The alveolar walls are congested.

(*b*) Can the action of the machine be regulated to prevent disturbance of the acid-base equilibrium of the body? At the beginning of our observations in the use of the respirator we were much concerned as to the proper pressures and the optimum rate of alternation

of pressure at which it was advisable to run the machine. Could it be regulated so as to avoid the development of alkalosis or acidosis? From our experiences with the cases reported here and with premature infants, we conclude that no nice relation exists between the rate and pressure of the machine and the quantitative ventilation of the lungs. For instance, a change of 10 per cent in the pressure

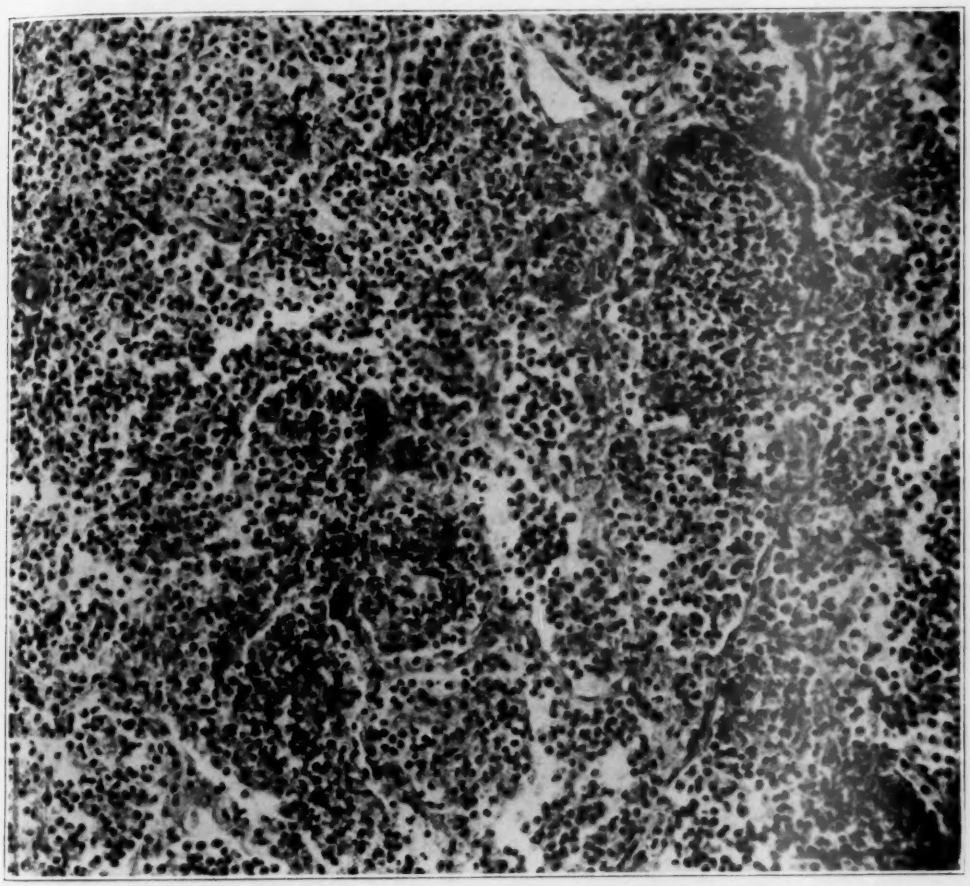

Fig. 4 (case 11).—Low power photomicrograph (hematoxylin and eosin stain) from a dependent portion of the lung. Diffuse bronchopneumonia is shown.

used does not necessarily mean a 10 per cent change in the amount of pulmonary ventilation.

We have frequently found, in children with simple paralysis of the intercostal muscles without pneumonia, that marked variations in the speed of the pressure cycles, and therefore of the rate of the induced respirations, ranging from 15 to 45 per minute, when made gradually,

would be accepted without any apparent discomfort. In most of the cases in children, however, rates of respiration between 20 and 30 per minute have been most satisfactory. The degree of negative pressure or vacuum in the respirator which is sufficient to produce inspiration in a paralyzed patient was determined only by experience. Negative pressures from 10 to 20 cm. of water during the inspiratory phase of the machine have been found satisfactory. By slowly changing the pressures while the paralyzed children were sleeping quietly, we found that they would usually become wakeful or restless when the pressure changes were reduced below 10 or raised above 20 cm. of water. At the higher pressures it could frequently be observed that resistance to the passage of air would be made, evidently by closing the glottis and thus obstructing inspiration or by holding the chest in inspiration, presumably likewise closing the glottis. This ability to resist successfully excessive ventilation we have seen even more prominently in infants who have been subjected for half an hour to pressures of 30 cm. (twice that usually employed) without more than a moment's subsequent apnea.

In only one of our cases have we observed any clinical evidence of overventilation, such as apnea when the machine is stopped, and we have not seen tetany from hyperventilation. In case 10, when the machine was stopped temporarily, the child did not breathe for thirty seconds. One cannot conclude, however, that this apnea was in compensation for a preceding overventilation of the lungs, because during periods of observation without the respirator the respiration of this child was excessively slow and irregular. Thus it seems that in the type of patient being studied, whether he was conscious or unconscious, there existed a fairly effective reflex mechanism that protected him against excessive hyperventilation. Governed only by observation of the patient's response to the action of the respirator, it was possible to choose fairly satisfactory pressures and speeds. It is quite possible, however, for the patient intentionally to allow himself to become hyperventilated. This possibility has been made use of in the treatment of adults [4] by running the machine at increased pressure and simultaneously administering oxygen and using the subsequent period of apnea as an opportunity to open the respirator and make changes in the bed-clothes and in the position of the patient.

3. *If life can be maintained by artificial respiration during the acute stage of poliomyelitis, will the patient with intercostal and diaphragmatic paralysis recover muscle power ultimately to an extent enabling him to live?*

The answer to this question was at first awaited with anxiety. If the paralysis, to the degree present at the acute stage, should be

4. Shambaugh, Harrison and Farrell (footnote 2).

permanent, we could not hope to accomplish anything. We would be forced to use the respirator indefinitely or until someone should turn executioner by stopping the machine, or until an intercurrent infection solved the problem for us. Judging by analogy from the course of the disease in other muscle groups it could be reasonably hoped that a considerable part of the extensive paralysis of the acute stage would prove temporary and that a relatively short time would allow the patient to recover enough to carry on by himself. This has so far in our experience proved to be the case. All of the children with intercostal or diaphragmatic paralysis have recovered sufficiently to breathe comfortably by themselves. The danger of hypostatic pneumonia, however, is considerable, as has been shown by the experience of others. We think that great stress should be laid on a systematic schedule for changing the position of the patient while in the respirator. With a patient who is entirely dependent on the machine for respiration, this may be difficult to do, but with carefully planned team-work it is quite possible to turn even a heavy patient first on one side and then on the other or even face downward. Protest on the part of the patient because of fear or tenderness should not prevent this plan from being conscientiously carried out.

4. *At what stage of the disease is the use of the machine indicated?*

To answer this question in respect to the children with paralysis of the respiratory muscles, the case of Elton B. (case 1) may be considered. In none of the patients was the respiratory paralysis complete. Each child, even in the acute stage, could carry on by himself for a few minutes. Elton B. was one of the least badly paralyzed. He was brought to us from a considerable distance by Dr. Aycock of the Harvard Infantile Paralysis Commission, who recognized, because of extensive and progressing paralysis involving both shoulders, that intercostal failure was probable. On arrival, the child was fatigued, would try to talk only in quickly whispered, short words, and then only on urging, was breathing rapidly with dilated alae nasae but was not definitely cyanotic, and was using only slightly his accessory muscles of respiration. There was paralysis of the intercostal muscles but probably not much involvement of the diaphragm. The child was given a sedative, made comfortable and left alone, but he did not sleep. After an hour, because we expected the paralysis might still extend, and in order to familiarize ourselves and him with the use of the machine, he was placed in the respirator. This caused the child some pain because of muscle tenderness. After about thirty seconds, time used in adjusting the rate and pressure of the machine, the child was noted to be apparently unconscious. Even a sharp stimulation did not arouse him. We were considerably disturbed at first by this

apparent "coma," but since his color was good and air passed freely in and out of the nostrils synchronously with the rhythm of the machine he was left alone. To be brief, we learned that the unconsciousness was only a deep sleep, that of utter fatigue. Since then we have seen the same phenomenon several times, an almost immediate deep sleep in spite of the excitement and sometimes pain involved in being first placed in the respirator, a sleep quite evidently due to the relief from the conscious voluntary attention to respiration necessary in these partially paralyzed conditions. In spite of the absence of such gross signs of anoxemia as cyanosis, and the absence of excessive use of the accessory respiratory muscles, we felt that we were giving real relief, and that further treatment in the respirator was indicated.

Since the importance of rest to any group of paralyzed muscles during the acute stage of poliomyelitis is now well recognized, we feel that the care of the respiratory muscles should presumably be no different from that of other groups. Cyanosis, the use of accessory muscles of respiration, and dyspnea, when due to paralysis, are very obvious indications for the use of the machine. With a machine available for use, we consider that much earlier signs should be watched for. Wakefulness, reduction of vital capacity as evidenced by monosyllabic, interrupted speech or rapid breathing, again if due to muscular weakness, justify a therapeutic trial to determine what relief can be given.

It is much more difficult to decide on the proper time to use the machine in patients with the purely bulbar type of respiratory embarrassment, or even whether to use it at all. Often only clinical trial makes us sure of our ground. Obviously here there is no question of early treatment as far as artificial respiration goes. The only justification for use of the respirator in the pure bulbar types is as a final desperate attempt to maintain life or as an immediate emergency in complete cessation of respiration (cases 7 and 8). The great value of postural drainage and the aid given by frequent aspiration of the pharynx, sometimes combined with a judicious use of atropine, must be emphasized. Nothing should be given by mouth to these children. An attack of vomiting should be considered very serious and should be prevented by every possible means. There is a great tendency to be overimpressed by the pharyngeal paralysis and to resort quickly to gavage feeding. We think this should be omitted until the fever and toxic symptoms have disappeared. We have found no difficulty in maintaining body fluids and preventing ketosis by the subcutaneous and intravenous injection of saline and dextrose solutions. At least not until every possibility of draining the pharynx has been attended to should the child be placed in the respirator, and then it should be inclined at as great an angle as possible. The possibility of aspiration

of material into the lungs is always present, and is made more likely by the use of morphine and the respirator. Only when the pharynx has been cleared as well as possible and when respirations become so inefficient that one feels justified in taking more desperate steps, do we consider the attempt justified to give aid with the machine. Then possibly the use of respiratory depressants such as magnesium sulphate and morphine may be considered worth while in an attempt to reduce the effect that the patient's spasmodic, ineffective, respiratory efforts have in preventing the efficient action of the respirator.

REPORT OF CASES

CASE 1.—Elton B., aged 10, became ill with fever, vomiting and pain in his back. Two days later he was noted to be breathing rapidly. Intercostal paralysis was recognized, and he was sent two hundred miles to the Children's Hospital where the only respirator at that time was available.

He was a very sick boy, watchful and alert, and he would speak only in single, quickly whispered syllables. He showed the stiff back and neck of poliomyelitis, complete paralysis of the intercostal muscles, probable weakness of the diaphragm and extensive paralysis of the arms and legs. There was no definite cyanosis, but the accessory neck muscles were brought into action on inspiration, and there was dilation of the nostrils.

After an hour's rest, during which he did not sleep, he was placed in the respirator. He went soundly to sleep there almost before the machine could be properly adjusted. He was kept in the respirator for fourteen days, gradually being allowed to stay in bed for longer intervals. At no time was he so completely paralyzed that he became definitely cyanotic when relying on his own respiratory efforts, but only after two weeks could he relax enough to sleep when out of the machine in his bed.

CASE 2.—Five days, and again two days before entry to the hospital, Harold F. had headache. The day of entry he had fever, weakness of legs and inability to void.

He appeared in a semistuporous state, had a stiff back and neck, some paralysis of both legs and evidently also of the bladder, which was markedly distended. The spinal fluid showed 55 cells per cubic millimeter, positive globulin and sugar tests. His condition remained essentially the same for two days and then became worse; his respirations became very irregular and of a spasmodic, jerking nature. There was no evident palatal or pharyngeal paralysis. His condition became so bad that without much hope of his obtaining aid he was finally placed in the respirator. To our surprise he was greatly helped; his respiratory efforts became regular and coincided with the rhythm of the machine, dyspnea became less and cyanosis disappeared. Whenever the machine was stopped, dyspnea reappeared. After two days in the machine we were sure that the intercostal muscles were paralyzed. Both arms were then discovered paralyzed. The results from the use of the machine were then understandable, though we had been at first quite confused by the unusual course and especially by the respiratory arrhythmia.

At one time during his treatment in the respirator, because of a fault in the manometer which measures the pressure used in the machine, he was subjected for some hours to an excessive pressure. The degree of pressure used was not known. He seemed quite comfortable and slept during this time, but the next

morning a moderate amount of subcutaneous emphysema appeared in his neck. This soon disappeared, however, without any evidence of having done harm.

The child eventually regained excellent use of his intercostal muscles.

CASE 3.—Eddie M., aged 4 years, had been ill for three days with fever and vomiting. On the third day weakness of the legs and arms was noted and increasing difficulty in breathing.

He was mentally alert, wide-eyed and frightened. There was a stiff neck and back, and paralysis of both shoulders, both legs and intercostal muscles. Little motion of the diaphragm could be detected. He was using his neck muscles and chin to aid breathing. There was moderate cyanosis. He would not try to speak except in an occasional whispered monosyllable.

He was placed in the respirator and immediately fell asleep. Relief from dyspnea appeared complete when he was asleep, but when awake he appeared very

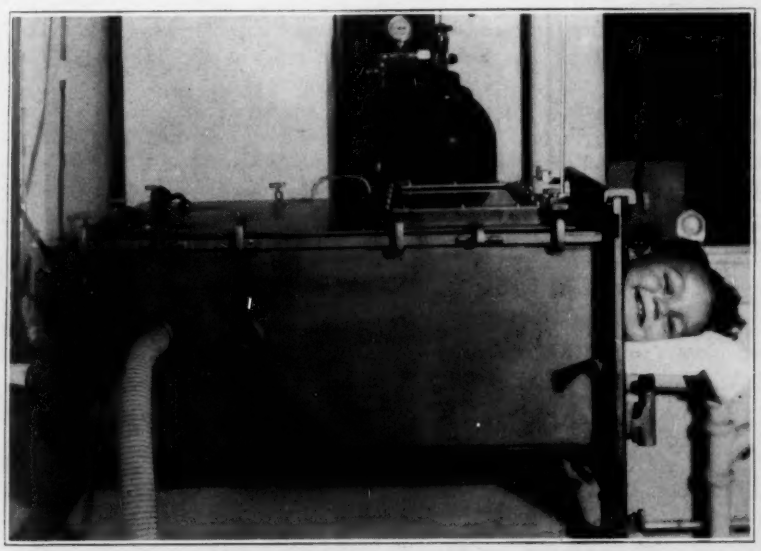

Fig. 5 (case 4).—Frank Z., aged 22 months, in an infant size respirator.

apprehensive and would begin to use his accessory muscles of respiration and his nostrils would dilate. His course was quite uneventful. After two weeks there was such recovery that he was gradually "weaned" away from the use of the machine which was needed for other patients.

CASE 4.—Frank Z., aged 22 months, had suffered from fever, vomiting and stiff neck for three days. On the day before admission to the hospital his left arm and leg were noted to be weak, and on the day of admission there was marked dyspnea.

On admission, he was extremely ill, cyanotic and very dyspneic. Both shoulders and one leg were paralyzed. There was motion of only the right side of the thorax on inspiration, and diaphragmatic action seemed affected. He was placed immediately in the respirator, but for some reason did not seem to be helped. In one hour, however, his condition was even worse, and the machine was tried again, with instant relief. A little later it was apparent that he was almost completely dependent on the machine and that his diaphragm was quite paralyzed.

The child was kept in the respirator except for a few minutes at a time for six weeks, then attempts were made gradually to discontinue the use of the machine. The muscle power returned only slowly, but by three months he was well enough to be discharged.

CASE 5.—Helen C., aged 4 years, had been quite well till eight days before admission to the hospital. At that time she became ill with headache, fever and vomiting. It was not until two days before entrance that it was noted that her arms were paralyzed. On the day of admission she had difficulty in breathing.

When first seen in the Children's Hospital she was very ill with marked evidence of loss of weight and tissue fluids. She was, however, very bright and alert, intently watching every motion around her. Her neck and back were held with marked resistance to flexion. There was evidently complete paralysis of the intercostal muscles, but the diaphragm moved fairly well. On inspiration, dilata-

Fig. 6 (case 5).—Helen C., aged 4 years, in an adult size machine. This was the first practicable respirator developed by Professor Drinker.

tion of the nostrils and use of the neck muscles was evident. The child spoke only with interrupted single syllables on each expiration. She was not cyanotic.

The child was not subjected to a lumbar puncture. After several hours' observation, during which she remained awake, she was placed in the respirator. There was considerable muscle tenderness, and the transfer from her bed caused pain. Within a minute after the respirator had been started she was fast asleep. Her breathing synchronized with the rhythm of the machine. The dilatation of the nostrils and the use of the accessory muscles of respiration ceased.

Helen was kept in the respirator for only one week. Her temperature became essentially normal after two days, during which her state of dehydration was actively combated. She learned quickly to talk and to swallow while the machine was running. Her disposition was charming. The dimples that she so readily displayed to every visitor and that the photographer caught so easily in pictures

(fig. 6) would immediately disappear, however, when the machine was momentarily stopped. After a week another child with more respiratory difficulty appeared, and as it was evident that by then Helen could breathe by herself well enough to live, she was taken from the machine, not without protest on her part.

CASE 6.—Warren E., aged 20 months, had been ill for four days with fever and vomiting. On the day of entrance to the hospital it was noted that he had difficulty in swallowing. His physician found a swelling of the right side of the pharynx and also a stiff neck and back.

On entrance, he appeared very sick. There was a moderately large swelling of the pharyngeal wall, and a small amount of pus was obtained on digital examination. The child could not swallow. There was a stiff back and neck. Lumbar puncture yielded fluid containing an increased number of cells, and the tests for globulin and sugar were positive. We were then sure that a pharyngeal paralysis existed, and that the difficulty in swallowing was not due to the pharyngeal infection.

The second day in the hospital the baby became more dyspneic and breathed irregularly with increasing cyanosis. He was placed in the respirator. There was immediate relief from symptoms. The next day, when the machine was stopped for a few moments to permit examination of the child, paralysis of the intercostal muscles and both arms and partial paralysis of the legs was discovered. The child was kept constantly in the respirator for about two weeks. He was very dependent on the machine. His diaphragm was only partially involved, but he could carry on respiration for only a short while by himself without cyanosis. Whenever the machine was stopped his pulse became immediately elevated to from 150 to 170 per minute, but would promptly fall again as soon as the machine was started.

After the second week he was kept in bed for increasing periods, but for two months he needed the respirator in order to sleep. He was given parenteral fluids only for the first few days, then was fed by gavage for almost three months. At one time during his second month in the hospital, when his nurse was attempting to teach him to swallow, he choked, became blue and stopped breathing. He was promptly placed in the respirator with immediate improvement in color, and after a few minutes again began to make spontaneous respiratory efforts.

CASE 7.—Conrad L., an Italian boy, had been ill for six days when he was referred to the hospital for relief from a possible foreign body in the esophagus. His illness had been at first characterized by fever, headache, generalized pains and vomiting. Soon it was noted that he had increasing difficulty in swallowing, choked when he attempted to take even fluids and was occasionally having difficulty in breathing.

On admission, the child presented a characteristic picture of acute poliomyelitis with pharyngeal paralysis. The spinal fluid gave a positive reaction to the globulin test and contained 60 cells per cubic millimeter.

Attempts were made by aspiration of his throat and by postural drainage to prevent attacks of choking, during which he would become quite cyanotic. Nothing was offered by mouth. He vomited frequently, however, and after one such attack spontaneous attempts at respiration ceased. After a few minutes, during which the usual manual artificial respiration was carried out, the child was placed in the respirator. The action of the machine was immediately effective, and there was marked improvement in color. The child soon became conscious. He was kept in the respirator part of the time for several days as he seemed to have better color and to rest more comfortably there. Although at one time an intercostal paralysis was considered present, the arms were not paralyzed, and

after two days good motion of the thorax was evident. The child made a complete recovery with no residual paralysis.

CASE 8.—Walter Z., aged 8 years, had been ill with fever, malaise, headache and vomiting for eight days. His course was characteristic of the "dromedary" type of poliomyelitis. He had been unable to swallow for twelve hours at the time of entrance to the hospital.

On entrance, he was slightly delirious and drowsy and exhibited the stiffness of back and neck characteristic of poliomyelitis. There was no paralysis found except of the pharynx and palate. He was unable to swallow and frequently choked severely on mucus in his pharynx. Aspiration of the pharynx was repeatedly resorted to. About twelve hours after entrance he had a severe choking attack and stopped breathing. He was placed in the respirator with immediate relief; his color again became normal. Throughout the next two days, except for short periods, he remained in the respirator. Although no paralysis was made out, he seemed much helped by the machine, even after regaining consciousness. His recovery was complete and, after the first two days, uneventful.

CASE 9.—Eight days before James M., 8½ years old, came into the hospital he woke up with a headache, sore throat and feverishness. After first improving a little, three days later he became worse, vomited and had pains in his back. After two more days he began to choke and have difficulty in swallowing. For the next few days he was treated for diphtheria and then was brought to the hospital.

On admission, he had pharyngeal and palatal paralysis, a stiff neck and back and a spinal fluid with an increased number of cells, and a positive reaction to the tests for globulin and sugar. For two days he did fairly well. Postural drainage, aspiration of throat, omission of all foods and fluids by mouth decreased the choking attacks. On the third day in the ward his respiration became irregular and jerky. Cyanosis increased. He was placed in the respirator for therapeutic trial, and rather to our surprise immediately improved. His respirations synchronized with the machine's rhythm. For the next four days his course was variable, periods of very irregular respiration alternating with sleep and relaxation. His only fluid intake was parenteral and by rectum.

For ten days there was improvement. Gavage feedings were tolerated without vomiting. Two weeks after entrance, bronchitis developed, and after a choking attack he again began to breathe very irregularly and inefficiently, with ensuing cyanosis. Though we did not understand the mechanism of this attack, he was placed in the respirator, again with prompt improvement. He was removed from the respirator after one day. From then on the course was uneventful. The child began to swallow seven weeks after entry. There was never at any time any paralysis detected except that of the palate and pharynx.

CASE 10.—Teresa S., aged 8½ years, was brought to the hospital after two days of increasing difficulty in breathing associated with inability to swallow. She had had some fever and headache for five days.

She was a well nourished little Italian girl, semiconscious, with moderate cyanosis, breathing relatively slowly with frequent interruptions due to choking. She had stiffness of the neck and back with a facial, palatal and pharyngeal paralysis.

After postural drainage and aspiration of the throat she seemed at first better, but soon her cyanosis deepened and she was placed in the respirator. She seemed definitely helped. There was excellent synchronism between her respiratory efforts and the rhythm of the machine. After a few hours, she was put to bed again.

Her respirations were very slow (10 to 12 a minute) but of moderate depth. There was no intercostal or diaphragmatic paralysis. After a half hour, because of considerable cyanosis, she was placed in the machine again, again with excellent results. Whenever the machine was stopped, her own respiratory rate would be extraordinarily slow, at times five a minute, and cyanosis would appear.

After two days her condition markedly improved, and she was returned to the ward and made a complete and uneventful recovery.

CASE 11.—Four days before coming to the hospital, Anna W. became ill with headache, fever, vomiting and pain in neck and back. The next day she was noticed to have a nasal voice, and when she drank, fluid regurgitated through her nose. During the two days before entry she experienced increasing difficulty in swallowing and in breathing.

At entry, she appeared conscious but severely ill. She breathed irregularly, frequently using the accessory muscles of respiration. There was moderate cyanosis. No true paralysis of the diaphragm or intercostal muscles or of the limbs was detected. She obviously had paralysis of the palate and pharynx. The spinal fluid showed an increased number of cells, an increase in globulin and a normal amount of sugar.

After attempts to clear her pharynx of fluids, she was placed in the respirator, by which, for a time, she seemed much helped. Irregular breathing, independent of any rhythm of the respirator, became more and more marked. She became unconscious. In desperation magnesium sulphate and morphine were given intramuscularly in an effort to so depress her respiratory center that the action of the respirator might be unopposed by her own spontaneous, jerky, inefficient and spasmodic respiratory efforts. For a time this seemed remarkably successful. However, on the fourth day of her treatment in the respirator her color became strikingly worse. Her pulse became rapid, thready and grossly irregular, and soon stopped.

CASE 12.—Richard D., aged 5, became ill three days before entrance to the hospital with fever and headache; the next two days these symptoms were combined with muscular pains and stiffness of back and neck. A nasal tone to the voice was noted.

On entrance, he appeared an alert, irritable, very ill child with definite weakness of shoulders and left arm. He presented the characteristic spasm of neck and back muscles. The spinal fluid showed an increased number of cells and a positive reaction to the tests for globulin and sugar. The second day in the hospital he became much worse. There was apparently an intercostal weakness and increasing respiratory difficulty. There was definite pharyngeal and palatal paralysis. Attacks of choking became frequent and respirations more and more irregular with resulting cyanosis. He was placed in the respirator with apparent relief at first. Soon, however, his respiratory efforts no longer coincided with the rhythm of the machine, his heart became more and more rapid and finally stopped.

CASE 13.—Mary D., aged 7, became ill three days before admission to the hospital. She complained of feverishness, headache and pain in her neck. For one day she had had a nasal voice and difficulty in swallowing.

She appeared mentally clear, but acutely ill with signs of meningeal irritation. There was a palatal and pharyngeal paralysis. Her spinal fluid contained 55 cells per cubic millimeter and gave a positive reaction to the tests for globulin and sugar. The day after admission, her respirations became irregular. She suffered from frequent choking attacks and cyanosis. She became so much worse that she

was placed in the respirator, but her spasmodic respiration prevented any aid being given. For a while it seemed that a large dose of morphine allowed the action of the machine to be more effective, but while the house doctor was feeling the temporal pulse, it suddenly stopped.

CASE 14.—Three days before entrance to the hospital, Norman D., aged 10 years, complained of headache and vomited. The day before entrance he had also a stiff neck, difficulty in swallowing and increasing difficulty in breathing.

On entrance, he was conscious but desperately ill and had a stiff neck and back characteristic of poliomyelitis. His palate, pharynx and right facial muscles were paralyzed. Respirations were irregular, jerky and accompanied by frequent choking attacks following vomiting. He was cyanotic. No paralysis of the respiratory muscles was made out. His spinal fluid showed 150 cells and gave a positive reaction to the tests for globulin and sugar. His blood pressure was 170 systolic and 110 diastolic under the conditions of examination. He seemed helped at first by postural drainage, aspiration of the throat and atropine. Soon his condition became so bad that the effects of the respirator were tried. There was no synchronism between his respiratory spasms and the rhythm of the respirator. His pulse became very rapid and thready, and soon stopped.

CASE 15.—Francis N., aged 4, was brought to us because of the onset of difficulty in swallowing and breathing occurring after two days' illness with fever and headache.

He appeared desperately ill, was semiconscious, cyanotic and breathing irregularly with frequent choking attacks. There was paralysis of the palate and pharynx, but no evidence of any weakness of other muscle groups. No lumbar puncture was done. Every effort was made to drain the pharynx by posture and by aspiration, and the child was then placed in the respirator.

He seemed at times to get definite aid from the respirator, but as a whole his respiratory efforts opposed that of the machine. His pulse became extremely rapid, and he soon died.

CASE 16.—Gwendolyn C., aged 7, became ill with fever, headache, backache and vomiting two days before being brought to the hospital, and on the day of admission had begun to "talk funny" and regurgitate fluids through her nose.

She was a beautifully developed child, alert and cooperative, with considerable tenderness on flexion of neck and back and with a palatal paralysis. Her spinal fluid contained 136 cells per cubic millimeter, and gave a positive reaction to the tests for globulin and sugar. On the second day in the hospital, she began to have evidence of pharyngeal paralysis and to breathe with more and more irregularity. She became less conscious, and cyanosis appeared. She was finally placed in the respirator, but with no evidence of deriving help. The rhythm of the respirator could not be made to coincide with her spasmodic breathing. Her pulse became faster and faster, and stopped in a few hours.

CASE 17.—Margaret B., aged 7 years, had been ill with fever and malaise for four days. For one day she had complained of pains in neck and back and had had trouble in swallowing and breathing for eight hours.

She was desperately ill on admission to the hospital, cyanotic, breathing irregularly and subject to frequent choking attacks. There was evidently paralysis of the pharynx alone. There was splinting of the neck and back. Her pulse was very rapid and thready.

A lumbar puncture yielded a fluid that gave a positive reaction to the Pandy test, contained 77 cells per cubic millimeter and gave a normal reaction to the test for sugar. Because of the child's desperate condition, with irregular, inefficient

respirations, after attempting to drain her pharynx by posture and by aspiration we placed her in the respirator. We were unable to regulate the rhythm of the machine to coincide with her respiratory spasms. She seemed no better or worse as the machine was started or stopped. Eight hours after entrance, her heart stopped. The respirator caused air to pass in and out of her lungs after death better than before.

NOTE.—Since this report was written twenty-five additional patients with respiratory failure due to poliomyelitis have been treated by means of the Drinker respirator. Experience with these additional patients, which is soon to be published, supports the conclusions drawn from an analysis of the cases herein reported.

CONCLUSIONS

1. In six children suffering from poliomyelitis who had paralysis of the intercostal muscles and the diaphragm without complications (such as pneumonia), the Drinker respirator was ideally efficient in maintaining pulmonary ventilation for long periods.

2. A therapeutic trial of the respirator seems desirable as soon as possible after any reduction of the vital capacity is discovered which is due to weakness of the respiratory muscles. Marked dyspnea or cyanosis should not be awaited as indications for initiation of treatment.

3. The action of the respirator seemed very effective in two children with bulbar paralysis without intercostal involvement who had a sudden complete cessation of respiration after choking.

4. The use of the machine seemed sometimes helpful but was often entirely ineffective in nine children with bulbar paralysis, without intercostal involvement, who had a disturbed central control of respiration manifested by irregular breathing. Only two of these nine children lived.

5. The use of the machine in cases with bulbar paralysis without intercostal involvement is not recommended except as an emergency and after every attempt has been made to free the pharynx from secretions.

6. It was not always possible to foretell accurately the effectiveness of the respirator before therapeutic trial.

7. Except for moderate emphysema found at necropsy in three patients with bulbar paralysis, no evidence of harm due to the use of the machine was discovered.

Dr. Lloyd Aycock and Dr. Sidney Kramer of the Harvard Infantile Paralysis Commission referred many of the patients from which the observations reported here were secured.

Warren Collins, Inc., and the Harvard Infantile Paralysis Commission loaned the Drinker respirator machines in which several of these patients were treated.

SEASONAL VARIATION IN ANTIRACHITIC ACTION OF ARKANSAS SUNSHINE

PAUL L. DAY, PH.D.
LITTLE ROCK, ARK.

A distinct seasonal variation in the antirachitic action of sunlight has been demonstrated by Tisdall and Brown at Toronto.[1] Similar variations have been shown in the ultraviolet intensities of sunshine at Baltimore [2] and Chicago [3] by photochemical rather than by biologic methods. On the other hand, Lewis, Frumess and Stein [4] have recently published data showing no such variation in the sunshine at Denver. The experiments on this subject published prior to 1930 together with the various methods employed have been carefully reviewed by Blunt and Cowan.[5]

Although severe rickets is less commonly found in the southern states than in northern cities, the incidence is far greater than can be justified in the light of the present knowledge of the etiology and prevention of this disease. Williams [6] wrote in 1928: "Severe rickets is extremely rare in New Orleans and vicinity, but a mild form of the disease prevails to the extent of about 45 per cent among children aged 3 years or less." More recently Mitchell [7] at Memphis examined five

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From the Department of Physiological Chemistry, School of Medicine, University of Arkansas.

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Mr. Charles J. Hart and Mr. William J. Darby assisted in this study.

1. Tisdall, F. F., and Brown, A.: Seasonal Variation of the Antirachitic Effect of Sunshine, Am. J. Dis. Child. **34**:721 (Nov.) 1927.

2. Clark, J. H.: The Zinc Sulphide Method of Measuring Ultra-Violet Radiation and the Results of a Year's Observations on Baltimore Sunshine, Am. J. Hyg. **9**:646 (May) 1929.

3. Tonney, F. O.; Somers, P. P., and Marti, W. C.: Actinic Measurement of Solar Ultra Violet Light and Some Correlations with the Erythema Dose, J. Prev. Med. **2**:493 (Nov.) 1928.

4. Lewis, R. C.; Frumess, G. M., and Stein, H. B.: A Comparison of the Antirachitic Effects of Winter and Summer Sunshine in Colorado, Am. J. Dis. Child. **41**:71 (Jan.) 1931.

5. Blunt, K., and Cowan, R.: Ultraviolet Light and Vitamin D in Nutrition, Chicago, University of Chicago Press, 1930.

6. Williams, C. T.: The Infrequency of Severe Rickets in New Orleans and Vicinity, Am. J. Dis. Child. **35**:590 (April) 1928.

7. Mitchell, F. T.: Incidence of Rickets in the South, South. M. J. **23**:228 (March) 1930.

hundred white and five hundred Negro children between the ages of 4 months and 4 years. Among the white children the incidence was found to be as follows: 11.2 per cent marked, 11.2 per cent moderate and 25.4 per cent mild rickets, a total incidence of 49.8 per cent. The prevalence of the disease among the Negro children was distinctly greater: 34.6 per cent marked, 34.8 per cent moderate and 18.2 per cent mild rickets, a total incidence of 87.6 per cent.

In the absence of prophylactic measures the antirachitic action of sunlight is an important factor in the prevalence of the disease. As data have not been available with regard to the variation in antirachitic effect of sunshine in this part of the country, the author has undertaken such an investigation. To this end experiments have been made at Little Rock almost continuously for the past two years, and more than four hundred rats have been employed in the determinations. Only the data obtained in the second year (June, 1930, to May, 1931) will be given here, as they confirmed and expanded the earlier experiments.

EXPERIMENTAL PROCEDURE

At the outset the general plan of the work was to determine, at different times of the year, the daily amount of sunshine necessary to prevent rickets in rats receiving a rachitic diet. For reasons stated later this method was slightly modified, and comparisons of the antirachitic effect of the sunlight at different seasons were made by determining the minimum daily amount of sunshine necessary for partial, but not complete, protection. All the animals employed in these experiments were reared in the author's laboratory from a stock of albino rats which for several generations had received Sherman's diet 13[8] with frequent additions of fresh lean meat and fresh lettuce. Healthy young from this colony, from 40 to 55 Gm. in weight, were placed in all-metal cages and given the Steenbock and Black rachitic diet 2,965.[9] Except for such times as they were being exposed to sunlight the animals were kept in a partially darkened room, fully protected from ultraviolet radiation. From two to four groups of eight animals each were used in each experiment, the rats being divided into groups with due regard to size, sex and litter. Suitable negative controls and positive controls receiving either cod liver oil or viosterol were employed in each experiment. On all clear days each group was given a definite predetermined amount of sunshine between the hours of 10 a. m. and 2 p. m. The average

8. Sherman, H. C., and Campbell, H. L.: Growth and Reproduction on Simplified Food Supply: IV. Improvement in Nutrition Resulting from an Increased Proportion of Milk in the Diet, J. Biol. Chem. **60**:5 (May) 1924.

9. Steenbock, H., and Black, A.: Fat-Soluble Vitamins: XXIII. The Induction of Growth-Promoting and Calcifying Properties in Fats and Their Unsaponifiable Constituents by Exposure to Light, J. Biol. Chem. **64**:263 (June) 1925.

daily exposure to sunlight was computed from the minutes of exposure and the number of days exposed. The experiments were terminated at the end of thirty days, the rats killed, the tibias removed and line tests made according to the usual technic.[10] The exposures to sunlight were made on a southern veranda of the two-story laboratory building where the animals received direct sunshine and light from a portion of the southern sky. The effective rays were probably not as intense there as they would have been on the roof, but as all the experimental animals were exposed in the same way, the results obtained at different seasons are directly comparable, although they may not be directly comparable to a series of experiments conducted in another city under a different set of conditions. The rats were exposed in cylindric cages, measuring 9 inches (22.8 cm.) by 9 inches, four animals to each cage. The sides and tops of the cages were built of hardware cloth of ½ inch (1.27 cm.)

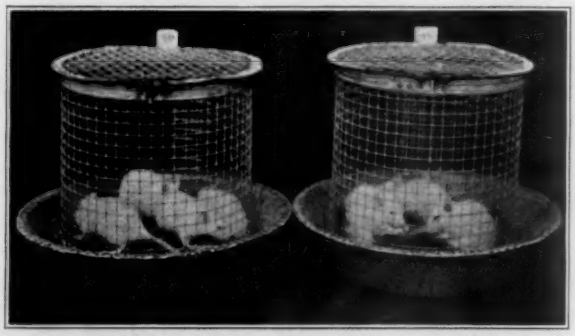

Fig. 1.—Two of the cages used in exposing the rats to sunshine. The tops and sides were built of hardware cloth of ½ inch mesh and the raised floors of hardware cloth of ⅜ inch mesh.

mesh and the raised floors of hardware cloth of ⅜ inch (0.87 cm.) mesh (fig. 1). It was not found necessary to use any method for warming the rats in winter. The building protected them from winds, and as they were exposed only on sunny days the temperature was always above freezing, and was usually comfortable for the animals. Rats exposed to the summer sun appeared to suffer more from heat than those exposed in winter did from cold.

Table 1 contains a summary of the data which were obtained in ten series of experiments of the second year of experimentation. On examination of the tibias each animal was assigned a line test value

10. McCollum, E. V.; Simmonds, N.; Shipley, P. G., and Park, E. A.: Studies on Experimental Rickets: XVI. A Delicate Biological Test for Calcium-Depositing Substances, J. Biol. Chem. **51**:41 (March) 1922.

of 1 +, 2 +, 3 + or 4 +, depending on the severity of rickets. According to this arbitrary scale, 1 + is slight protection against rickets, while 4 + is complete protection, that is, no evidence of rickets. The average line test for a group, as shown in the right hand column of table 1, was obtained by averaging the values for the component members of that group. A 2 + line test has been chosen as a basis of comparison for these experiments. In their critique of the line test for vitamin D,

TABLE 1.—*Summary of Data Showing the Effects of Graded Exposures to Sunlight on Rats Receiving a Rachitic Diet, at Different Times of the Year*

Dates	Average Daily Exposure, Minutes	Number of Rats	Average "Line Test"
May 30 to June 28, 1930	5	8	1.9+
	10	8	2.9+
	15	8	3.9+
	20	6	4.0+
June 14 to July 14, 1930	5	8	2.2+
	10	7	3.0+
	15	8	3.6+
Sept. 13 to Oct. 11, 1930	5	8	0.4+
	10	8	0.7+
	15	8	1.6+
	20	8	2.6+
Oct. 11 to Nov. 10, 1930	30	9	1.2+
	60	9	1.9+
	90	9	2.5+
	114	9	3.1+
Oct. 30 to Nov. 29, 1930	35	7	0.9+
	70	8	1.7+
	90	8	2.1+
	135	8	2.4+
Dec. 1 to 31, 1930	120	8	1.8+
	168	11	2.1+
Jan. 1 to 30, 1931	120	7	2.1+
	153	8	2.2+
Feb. 8 to March 10, 1931	40	8	1.4+
	80	8	2.0+
	120	8	2.6+
March 26 to April 25, 1931	15	8	1.7+
	30	8	3.0+
	45	7	3.1+
	60	7	3.4+
April 23 to May 23, 1931	5	8	1.9+
	10	8	2.8+
	20	6	4.0+

Bills and his co-workers [11] stated: "It is evident . . . that the line test is most critical between 1 + and 2 + healings." Although in this work the method used was protective rather than curative, it seems probable that the same rule would hold true. The other logical method of comparison, that is, the amount of sunlight necessary to afford complete protection, would be impossible in these experiments, as for several months of the year there was not enough sunlight available, under the

11. Bills, C. E.; Honeywell, E. M.; Wirick, A. M., and Nussmeier, M.: A Critique of the Line Test for Vitamin D, J. Biol. Chem. **90**:619 (Feb.) 1931.

conditions of the experiments, to afford anything like complete protection against rickets.

In table 2 the data are summarized by listing the average daily exposure to sunlight necessary to produce an approximate 2 + line test at the different months of the year, and in figure 2 the same results are plotted graphically. The time will be seen to vary from five minutes daily in May, June and July to one hundred and sixty-eight minutes daily in December, with intermediate values for the months between.

TABLE 2.—*The Average Daily Exposure to Direct Sunlight at Little Rock Necessary to Give Partial Protection (2+ Line Test) Against Rickets in Rats Receiving a Rachitic Diet, at Different Times of the Year*

Date	Exposure, Minutes
June, 1930	5
June–July, 1930	5
September, 1930	15
October, 1930	60
November, 1930	90
December, 1930	168
January, 1931	120
February, 1931	80
April, 1931	15
May, 1931	5

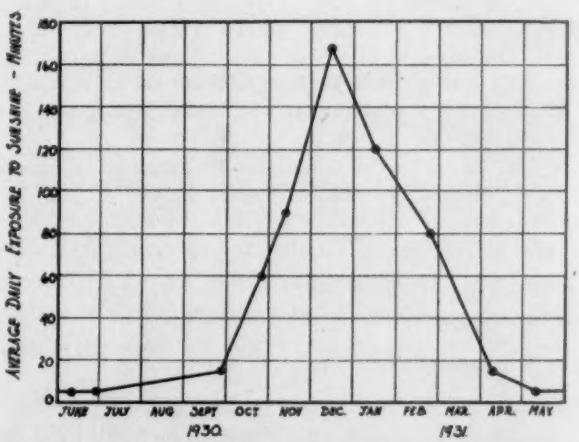

Fig. 2.—Seasonal variation in antirachitic action of sunshine at Little Rock. The points plotted represent the average daily exposure to direct sunlight necessary to afford protection sufficient to give a 2+ line test in rats receiving a rachitic diet.

As would be expected, the curve is roughly the inverse of a curve of the altitudes of the sun. It is evident that winter sunshine at Little Rock has slight but definite antirachitic action, and although the differences in methods of determination used make absolute comparisons impossible, it appears that the intensity of the active rays in winter sunshine here is of about the same order as has been found at Toronto,[1]

Boston,[12] New York [13] and Washington,[14] but is decidedly inferior to Denver [4] sunshine in this respect. The lower incidence of severe rickets in the South is probably due in part to the milder climate, which permits the infant and child to spend more time outdoors, with less clothing, in the autumn, winter and spring than is possible in more severe climates.

Although it is impossible at the present state of knowledge to translate rat requirements into infant requirements, the tentative conclusion seems warranted that sunshine at Little Rock from November to February, inclusive, is not satisfactory as a sole source of the antirachitic factor.

SUMMARY

Biologic determinations of the antirachitic action of sunshine have been made at Little Rock at all times of the year with large groups of animals under carefully controlled conditions. The average daily amount of sunshine necessary to afford the same partial protection against rickets in rats receiving a rachitic diet varied from five minutes in May, June and July to one hundred and sixty-eight minutes in December, with intermediate values for the other months.

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12. Wilder, T. S., and Vack, C.: Antirachitic Effect of Winter Sunshine Through Celoglass, Am. J. Dis. Child. **39**:930 (May) 1930. Wyman, E. T.; Drinker, P., and MacKenzie, K. H.: Antirachitic Value of Winter Sunlight in the Latitude of 42° 21′ (Boston), Am. J. Dis. Child. **39**:969 (May) 1930.

13. Eddy, W. H.: The Use of Ultra-Violet Light Transmitting Windows, Am. J. Pub. Health **18**:1470 (Dec.) 1928.

14. Fleming, W. D.: The Anti-Rachitic Efficiency of Winter Sunlight of Washington, D. C., Mil. Surgeon **62**:592 (May) 1928.

TREATMENT OF CONGENITAL SYPHILIS WITH ACETARSONE (STOVARSOL) GIVEN BY MOUTH

C. H. MAXWELL, JR., M.D.
AUBURN, N. Y.
AND
JEROME GLASER, M.D.
ROCHESTER, N. Y.

During the winter of 1929, while attending postgraduate clinics in Europe, the opportunity was given one of us (Dr. Glaser) to observe the treatment of patients with congenital syphilis with acetarsone administered by mouth. The enthusiasm with which this drug was recommended by such eminent pediatricians as Pirquet, Knöpfelmacher, von Reuss and Leiner of Vienna, and Finkelstein, Czerny, Meyer and Rosenstern of Berlin, as well as published reports from other Austrian and German clinics, led us to undertake the investigation here reported.

HISTORICAL DATA

Ehrlich apparently first prepared 3-amino-acetyl-4-hydroxyphenyl-arsonic acid as 594 in the series of investigations that led to the discovery of 606 (arsphenamine). We have been unable to find the records of Ehrlich's experiments with "594," and Raiziss [1] stated that no authentic account by Ehrlich concerning it exists. Bauer and Benda [2] stated that Ehrlich discovered "594" in 1909, but that it was little used because it was overshadowed in its therapeutic effect by arsphenamine. Kolle [3] made practically the same statement.

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From the Department of Pediatrics, the University of Rochester School of Medicine and Dentistry, and the Strong Memorial Hospital and the Genesee Hospital, Rochester, N. Y.

The acetarsone (stovarsol) used in this work was provided through the courtesy of Merck & Company.

1. Raiziss, G. W.: Personal communication to the authors.

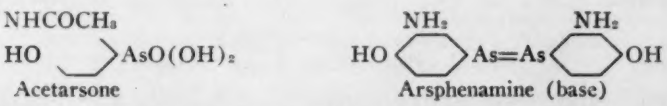
2. Bauer, H., and Benda, L., in Kolle, W., and Zeiler, K.: Handbuch der Salvarsantherapie, Berlin, Urban & Schwarzenberg, 1924, vol. 1, p. 379.

3. Kolle, W.: Ueber die Schutzwirkung der Antisyphilitika (Arsenderivate, Quecksilber und Wismut) gegenüber der experimentellen Syphilisinfektion, Deutsche med. Wchnschr. **50**:1074 (Aug. 8) 1924.

In 1921, the antisyphilitic properties of the drug were reinvestigated in France through the efforts of Fourneau.[4] The early experiments were with 3-amino-4-hydroxyphenylarsonic acid or 593 of Ehrlich's series. This preparation was known as 189 of Fourneau's series. Later the acetylated form, 190 of Fourneau's series (594 of Ehrlich), was the drug most used. Apparently Fourneau gave the name stovarsol to this preparation, though the first mention of the term is by other authors[5] who used the drug experimentally in syphilis at Fourneau's suggestion. Levaditi and Navarro-Martin,[6] using the sodium salt of this drug, demonstrated its effectiveness when given by mouth in the prevention and treatment of syphilis in man and animals. Further experiments[7] tended to corroborate this, not only with the sodium salt, but with the original drug.

PHARMACOLOGY AND TOXICOLOGY

Ehrlich's 594, known in France as stovarsol, in Germany as spirocid and in Russia as osarol, has been accepted in "New and Nonofficial Remedies"[8] by the Council on Pharmacy and Chemistry of the American Medical Association as acetarsone. It is a pentavalent arsenic compound, and its structural formula as compared to arsphenamine is as follows:



Acetarsone — Arsphenamine (base)

Acetarsone is a white, odorless powder, having a slightly acid taste; is slightly soluble in solutions of alkalis or alkaline carbonates; is stable at ordinary temperatures, and contains from 27.1 to 27.4 per cent arsenic, whereas neoarsphenamine contains 20 per cent and arsphen-

4. Fourneau, A.: Sur l'emploi de l'acide oxyaminophénylarsinique et des acides arylarsiniques en général dans le traitement des spirilloses et des trypanomiases, Ann. Inst. Pasteur **35**:571 (Sept.) 1921.

5. Levaditi, C.; Navarro-Martin, L.; Fournier, L.; Guénot, L., and Schwartz, A.: Recherches sur l'action curative et préventive de l'acide acétyloxyaminophénylarsinique (190 ou stovarsol) administré par voie digestive dans la syphilis, Ann. Inst. Pasteur **36**:729 (Nov.) 1922.

6. Levaditi, C., and Navarro-Martin, A.: Action therapeutique de l'acide oxyaminophénylarsinique dans la spirillose des poules et la syphilis expérimentale du lapin, Ann. Inst. Pasteur **36**:46 (Jan.) 1922.

7. Fournier, L.; Guénot, L., and Schwartz, A.: Premiers résultats du traitement de la syphilis par l'acide oxyaminophénylarsinique (sel de soude) ou "189," Ann. Inst. Pasteur **36**:53 (Jan.) 1922. Levaditi, C., and Navarro-Martin, A.: Action préventive et curative dans la syphilis du dérivé acétyle de l'acide oxyaminophénylarsinique (sel de soude), Compt. rend. Acad. d. sc. **174**:893 (March 27) 1922.

8. New and Nonofficial Remedies, Chicago, American Medical Association, 1930, p. 73.

amine 32 per cent. The French, German, Russian and American chemists manufacture the drug in 0.25 Gm. tablets.

Chen, Anderson and Leake [9] have shown that the ingestion of acetarsone is followed by rapid excretion of arsenic in the urine. Raiziss and Severac [10] introduced the spirochetes of syphilis into the subarachnoid space intracranially in rabbits and then gave either acetarsone or tryparsamide intravenously Acetarsone was apparently more effective in preventing the development of syphilis in doses one-third as large as those of tryparsamide. Raiziss, Severac and Moetsch [11] reported their own work and the work of other authors on the toxicity of acetarsone experimentally in rabbits and rats, as indicated in tables 1 and 2.

TABLE 1.—*Toxicity of Acetarsone in Rabbits When Given by Mouth*

Preparation	Dose per Kilogram of Body Weight	
	Maximum Tolerated, Gm.	Lethal, Gm.
Acetarsone "A" (made in America)	1.0	1.5
Acetarsone "B" (made in America)	0.4	0.5
Levaditi and Navarro-Martin (French preparation)	0.3-0.4	0.66
Poole (French preparation)	...	0.20
Collier and Evers (German preparation)	Less than 0.05	0.10
Schlossberger (Ehrlich's acetarsone)	...	0.10

TABLE 2.—*Toxicity of Acetarsone and Its Sodium Salt Administered Intravenously*

Preparation	Dose per Kilogram of Body Weight			
	Rats		Rabbits	
	Maximum Tolerated, Gm.	Lethal, Gm.	Maximum Tolerated, Gm.	Lethal, Gm.
Acetarsone "A"	0.25	0.3	0.1	0.12
Acetarsone "B"	0.30	0.4	0.5	....
Sodium salt of acetarsone "A"	0.70	0.75	0.5	0.6
Sodium salt of Ehrlich's acetarsone (Collier and Evers)	....	....	0.3	0.4

Leake, Koch and Anderson [12] found the minimum lethal dose of acetarsone "A" to be from 125 to 150 mg. per kilogram for rabbits and

9. Chen, M. Y.; Anderson, H. H., and Leake, C. D.: Rate of Urinary Arsenic Excretion After Giving Acetarsone and "Carbarsone" by Mouth, Proc. Soc. Exper. Biol. & Med. **28**:145 (Nov.) 1930.

10. Raiziss, G. W., and Severac, M.: Chemotherapeutic Studies Concerning the Penetration of Organic Compounds of Arsenic into the Cerebrospinal System, Arch. Dermat. & Syph. **22**:1031 (Dec.) 1930.

11. Raiziss, G. W.; Severac, M., and Moetsch, J. C.: Toxicity of Acetarsone (Stovarsol), J. Chemotherapy **7**:1 (April) 1930.

12. Leake, C. D.; Koch, D. A., and Anderson, H. H.: Effect on Biological Activity of Substituting Sulphur for Oxygen in Organic Arsenical Compounds, Proc. Soc. Exper. Biol. & Med. **27**:717, 1930.

from 150 to 175 mg. for cats. At autopsy, these animals showed distention of the stomach, large intestines and bladder; congestion of the lungs, liver and kidneys, and occasional hemorrhages in the kidneys; tubular degeneration of the kidneys; deposition of pigment in the lungs, liver and kidneys; disorganization of the muscle fibers of the stomach, and liver cells filled with fat globules.

The toxic effects noted have been more frequent but less serious than those accompanying the use of arsphenamine. Various authors [13] reported the development of: coryza, bronchitis, sore throat, malaise, aching, chill, fever, abdominal pain, jaundice, adenitis, urticaria, edema, albuminuria, eosinophilia, leukopenia and pruritic anal eczema.[14] The skin eruptions noted have varied from a scarlatiniform or a measles-like rash to a mild exfoliative dermatitis.[15] Measles may be so closely simulated by the malaise, lacrimation, coryza, fever, leukopenia and rash that a differential diagnosis is difficult, especially since Koplik's spots [16] have been reported as a part of the reaction.

The drug has been used for such a relatively short time that the reports on its toxicity are not numerous enough to indicate definitely just how many of the foregoing conditions are genuine toxic effects of the drug or due merely to coincidence.

The toxic effects reported have been much less frequent in infants than in older children or in adults. They will be discussed subsequently.

There is marked variation in the individual susceptibility to the drug. Cregor and Gastineau [17] reported that some of their patients

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13. Anderson, H. H., and Leake, C. D.: Toxicity of Acetarsone and Its Calcium and Sodium Salts on Oral Administration to Dogs and Cats, Proc. Soc. Exper. Biol. & Med. **27**:267, 1930. Izar, G.: Caractères de l'hypersensibilité au stovarsol, Paris méd. **2**:139 (Aug. 8) 1925. Bender, W. L.: Stovarsol (Spirocid) Poisoning: Report of Six Cases, Am. J. M. Sc. **174**:819 (Dec.) 1927. Porot, A.: Troubles sensitifs et pseudo-tabes dus à l'emploi du stovarsol par voie buccale, Bull. et mém. Soc. méd. d. hôp. de Paris **46**:140 (Feb. 10) 1930. Schereschewsky, J.: Zur Spirocidfrage, Deutsche med. Wchnschr. **56**:662, 1930. Jausion H., Langin and Gauch: Leuco-mélanodermie généralisée post-érythrodermique après cure au stovarsol, Bull. Soc. franç. de dermat. et syph. **37**:552 (May) 1930. Herz, W.: Zur Frage der Spirozidschädigung, Deutsche med. Wchnschr. **56**:1483 (Aug. 29) 1930.

14. von Bassewitz, E.: As-Dermatitis in Form des pruriginösen Analekzems, München. med. Wchnschr. **76**:743, 1929.

15. Michael, J. C.: Exfoliative Dermatitis from Acetarsone (Stovarsol), J. A. M. A. **92**:645 (Feb. 23) 1929.

16. Harrison, C. H.: The Treatment of Chronic Amebic Dysentery and Ameba Carriers with Stovarsol, U. S. Vet. Bur. M. Bull. **2**:447, 1926.

17. Cregor, F. W., and Gastineau, F. M.: Stovarsol in the Treatment of Syphilis, Arch. Dermat. & Syph. **16**:43 (Jan.) 1927.

(syphilitic adults) received as much as 2.25 Gm. of the drug daily for four days without any untoward effects. Oppenheim,[18] on the other hand, reported a Jarisch-Herxheimer reaction following 30 mg. of acetarsone.

We got the impression from the literature that in giving acetarsone fewer serious reactions are encountered if small doses are given to start with and are gradually increased.

CONDITIONS OTHER THAN SYPHILIS

Acetarsone is contraindicated in lymphogranulomatosis, according to Opitz,[19] who tried it in three cases in children. Two children died, and at autopsy one showed the typical picture of cerebral purpura such as is seen in arsphenamine poisoning; the second showed acute congestion of the brain with microscopic hemorrhages. These are the only cases in which autopsy reports were found. The third child recovered after a stormy convalescence.

In amebic dysentery,[20] acetarsone has been used widely and apparently successfully. In ulcerative colitis, from which amebae have not been isolated, Pulsifer [21] reported improvement in sixteen cases coincident with the administration of the drug. Favorable results are reported in pemphigus,[22] yaws,[23] intestinal lambliasis [24] and the spirillary diseases: intestinal spirochetosis,[25] ulceromembranous stomatitis,[25]

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18. Oppenheim, M.: Spirocid (Stovarsol) bei Syphilis, Arch. f. Dermat. u. Syph. **151**:306, 1926.

19. Opitz, H.: Zur Anwendung des Spirozids bei Lymphogranulomatose, Deutsche med. Wchnschr. **56**:659 (April 18) 1930.

20. Marchoux, E.: Le stovarsol guérit rapidement la dysentérie amibienne, la lambliase, et autres parasitoses, Presse méd. **33**:299 (March 7) 1925. Petzetakis: Le stovarsol dans le crise aiguë de la dysentérie amibienne, la lambliase et autres parasitoses, Presse méd. **33**:299 (March 7) 1925. Johns, F. M., and Jamison, S. C.: The Treatment of Amebiasis by Oral Administration of Stovarsol, J. A. M. A. **84**:1913 (June 20) 1925. Craig, C. F.: Symptomatology, Diagnosis and Treatment of Carriers of Endameba Histolytica, J. A. M. A. **90**:1345 (April 28) 1928. Harrison (footnote 16).

21. Pulsifer, L.: Personal communication to the authors.

22. Kromayer: Sechs durch Spirozid geheilte Pemphigusfälle, Deutsche med. Wchnschr. **55**:229 (Feb. 8) 1929.

23. Baermann, G.: Die schützende Wirking von "Stovarsol" bei Framboesia tropica, Arch. f. Schiffs- u. Tropen-Hyg. **27**:229, 1923. Tanon and Jamot: Le traitement du pian par le stovarsol, Rev. de méd. et d'hyg. trop. **16**:18, 1923.

24. Marchoux, E.: Action du stovarsol contre les lambliases, Bull. Soc. path. exot. **16**:325 (May 9) 1923. Petzetakis (footnote 20).

25. Levaditi, C.: Therapeutic Properties of Stovarsol, Lancet **2**:593 (Sept. 19) 1925.

spirillary bronchitis,[26] phagedemic ulcer [27] and Vincent's angina.[28] It has been used in trypanosomiasis [29] and as a vermifuge.[30]

The reports on the treatment for malaria [31] vary, but it is generally agreed that the drug is effective only in the tertian type; that relapses are frequent, and that its principal use should be in pregnancy or in other conditions in which quinine cannot be tolerated. In dementia paralytica in which malarial infection is intentional acetarsone has given satisfactory results in curing the malaria.

The tonic effect of acetarsone has been commented on by various authors, and patients report a feeling of well-being when taking the drug. Levy [32] has used the drug in convalescents and Tenzer [33] in poorly thriving nonsyphilitic infants for its so-called "tonic" effect. Although good results are reported, both authors have given treatment in small uncontrolled series of cases.

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26. Couvy, L.: Un cas de bronchite fétide traité par le stovarsol, Bull. Soc. path. exot. **17**:533 (July 9) 1924.

27. Couvy, L.: Le stovarsol dans l'ulcère phagédénique, Bull. Soc. path. exot. **17**:531 (July 9) 1924.

28. Couvy, L.: Le stovarsol dans l'angine de Vincent, Bull. Soc. path. exot. **17**:530 (July 9) 1924. Hutter, F.: Ueber die Behandlung der Plaut-Vincentschen Angina und anderen Spirillosen der Mundhöhle mit Spirocid, Wien. klin. Wchnschr. **40**:192 (Feb. 10) 1927. Rosenbaum, H. A.: Treatment of Vincent's Angina and Stomatitis, Illinois M. J. **59**:375 (May) 1931.

29. Fourneau, A., and Navarro-Martin, A.: Traitement des trypanosomiases expérimentales par les acides oxyaminophénylarsiniques, Compt. rend. Soc. de biol. **87**:1197 (Dec. 9) 1922. Fourneau, A.; Navarro-Martin, A., and Tréfouel, J.: Les dérivés de l'acide phénylarsinique (arsenic pentavalent) dans le traitement des trypanosomiases et des spirilloses expérimentales, Ann. Inst. Pasteur **37**:551, 1923. Navarro-Martin, A.: Sur l'emploi de l'aminophénolarsinate de soude dans le traitement des trypanosomiases, ibid. **36**:38 (Jan.) 1922.

30. Labernadie, V.: Le stovarsol comme vermifuge, Rev. d. méd. et d'hyg. trop. **21**:188, 1929.

31. Marchoux and Cohen: Le stovarsol est, contre le paludisme au moins aussi actif que la quinine, Compt. rend. Soc. de biol. **92**:132 (Jan. 24) 1925. Marchoux, E.: Action de l'arsenic sur le paludisme à P. vivax, Compt. rend. Soc. de Acad. d. sc. **180**:617 (Feb. 23) 1925. Sinton, J. A.: Studies in Malaria with Special Reference to Treatment, Indian J. M. Research **15**:287 (Oct.) 1927. Dupuy, H.: Un cas de fièvre bilieuse hémoglobinurique de nature nettement plaudéenne, traité par le stovarsol, Bull. Soc. path. exot. **21**:636, 1928. Freiman, M.: Stovarsol in Treatment of Malaria, J. Trop. Med. **30**:127 (May 16) 1927. Bass, C. C.: Treatment of Malaria with Reference to Recently Promoted New Remedies, J. A. M. A. **95**:988 (Oct. 4) 1930.

32. Levy, A. A.: Some Therapeutic Applications of a New Calcium Stovarsol Phosphate Combination, M. J. & Rec. **129**:279 (March 6) 1929.

33. Tenzer, O.: Ueber die ansatzförderende Wirkung des Stovarsols bei schlecht gedeihenden, nicht luetischen Säuglingen, Monatschr f. Kinderh. **34**:6, 1931.

Gourvitsch,[34] thinking that epidemic parotitis might be caused by a spirochete, tried acetarsone in twenty cases, apparently with good results. Children from 6 to 7 years old received from 0.15 to 0.20 Gm. of the drug daily.

ADULT SYPHILIS

In the prophylaxis of adult syphilis, acetarsone has more enthusiastic advocates than it has for the treatment for the disease in adults. Oppenheim [35] believed that we have no better prophylactic than acetarsone, and he considered it more effective than arsphenamine in this regard. On a scale of 10, he scored acetarsone 10 and arsphenamine 8. He used three tablets a day for three days. In a later paper, he reported the use of acetarsone with bismuth in the prophylaxis of syphilis at all ages. In all the cases in which the serum reaction was negative at the start, it remained negative during the period of observation up to one and one-half years.

In the treatment for adult syphilis, the drug has been used widely abroad, Oppenheim [36] reporting the treatment in over five hundred cases, and Levaditi, Fournier, Guénot, Navarro-Martin and Schwartz [37] in eighty cases; Cregor and Gastineau [17] reported the treatment in fifteen cases in Indianapolis (apparently the first American paper on the treatment for syphilis with acetarsone). There is some evidence also to show that acetarsone may be beneficial in dementia paralytica.[38] Sézary and Pomaret,[39] Yavonowitch,[40] Spiethoff,[41] Luerssen [42] and Scherber [43] have also written on the use of acetarsone in adult syphilis.

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34. Gourvitsch, I.: Die Behandlung von Mumps mit Spirocid, Arch. f. Kinderh. **84**:228 (June 15) 1928.

35. Oppenheim, M.: Die Indikationen des Stovarsols (Spirocid) bei der Behandlung der Lues, Wien. med. Wchnschr. **76**:918, 1926; Die interne Behandlung der Syphilis mit Stovarsol oder Spirozid, Klin. Wchnschr. **6**:1291 (July 2) 1927.

36. Oppenheim (footnote 35, second reference).

37. Levaditi, Navarro-Martin, Fournier, Guénot and Schwartz (footnote 5). Sézary, A., and Barbé, A.: Résultats cliniques et biologiques de la Stovarsolthérapie dans 125 cas de paralysie générale, Presse méd. **37**:1 (Jan. 2) 1929.

38 Sézary and Barbé (footnote 37).

39. Sézary, A., and Pomaret, M.: L'action antisyphilitique et spirillicide de l'acide acétaloxyaminophénylarsinique (190 de Fourneau), Bull. et mém. Soc. méd. d. hôp. de Paris **47**:318 (Feb. 23) 1923; L'action spirillicide des composés arsinicaux 914 et 190 administrés par voie buccale, ibid. **47**:595 (April 30) 1923.

40. Yavonowitch, M. D.: Le stovarsol: Ses indications thérapeutiques, Thèse de Paris, 1924.

41. Spiethoff, B.: Erfahrungen mit dem Stovarsol, Med. Klin. **21**:201 (Feb. 6) 1925.

42. Luerssen: Die Behandlung der Syphilis mit Stovarsol (Spirocid), insbesondere dessen Wirkung auf Spirochäten, Klin. Wchnschr. **4**:699 (April 9) 1925.

43. Scherber, G.: Die innere Behandlung der Syphilis mit Spirozid, Wien. klin. Wchnschr. **40**:813 (June 23) 1927.

In general, the methods of treatment are similar: From 2 to 4 tablets (0.5 to 1 Gm.) are given daily for from five to seven days, followed by a rest period of equal length to allow for elimination of the drug. The course is repeated again and again.

Most of the writers agree that acetarsone is best given in combination with bismuth or mercury. Except for Gitman,[44] the writers also seem to agree that acetarsone is not as effective as arsphenamine. Oppenheim,[36] in comparing the two in the treatment for adult syphilis, scored acetarsone 4 in a scale of 10 and arsphenamine 10. However, he [45] stated that no other medicine given by mouth in syphilis approaches acetarsone in effectiveness.

All investigators agree that acetarsone has beneficial effects in adult syphilis. The indications most generally agreed on for its use apparently are:

1. Hypersensitiveness to arsphenamine.
2. Difficulty in giving intravenous therapy.
3. Impossibility of treatment other than by mouth.
4. Syphilitic aortitis.
5. Syphilitic nephritis.
6. Gumma of the mouth, pharynx and larynx.
7. Country districts where regular attendance at a clinic is extremely difficult, especially in the winter months. Apparently some physicians send patients away with a course of acetarsone with or without instructions to discontinue the use of the drug in case of toxic symptoms. The toxic symptoms are ordinarily so mild that therapy is not interrupted.

CONGENITAL SYPHILIS

Not even the advocates of acetarsone for amebic dysentery are as enthusiastic as those who use the drug for congenital syphilis. They are astonishingly in agreement.

The treatment for congenital syphilis with acetarsone was first reported in 1924 by Dupérié, Cadenaule and Clarac.[46] They recorded good results in the treatment of a syphilitic infant 2 months old, a child who was a twin of a macerated fetus. They also mentioned another congenitally syphilitic infant treated with good results by other

44. Gitman, S. M.: Osarol (Acetarsone) in Syphilis, Venerol. i dermat. **7**:17 (Jan.) 1930.

45. Oppenheim, M.: Spirocid (Stovarsol) bei Syphilis, Arch. f. Dermat. u. Syph. **151**:306, 1926.

46. Dupérié, R.; Cadenaule, P., and Clarac, J.: Sur un cas de syphilis héréditaire précoce traité par le stovarsol ou 190, Gaz. hebd. d. sc. méd. de Bordeaux **45**:456 (July 20) 1924.

physicians. Somewhat later in the same year, Krösl [47] reported seventy-three cases of syphilis in which the patients were treated with acetarsone; three of these cases were in infants with congenital syphilis. Only one of

TABLE 3.—*Effects and Dosage of Acetarsone as Reported by Various Authors*

Authors	No. of Cases	Dosage	Effect on Wassermann Reaction	Toxic Effects
Klaften, E.: Zentralbl. f. Gynäk. **51**: 400, 1927; Klin. Wchnschr. **7**: 458, 1928	12	15 Gm. with mercury	Favorable	Frequent but not severe Herxheimer reaction; vomiting
von den Steinen, R.: München. med. Wchnschr. **74**: 1006, 1927	10	10-15 Gm. in 3 mos.	8 of 9 reversed in 3 to 4 months	
Soldin, M., and Lesser, F.: Deutsche med. Wchnschr. **54**: 958, 1928; Arch. f. Dermat. u. Syph. **160**: 198, 1930	46	30-50 Gm.	7 cases negative with 15 Gm. in 2 months; 2 cases negative with 20 Gm. in 9 weeks; 3 cases negative with 25 Gm. in 10 weeks; 1 case negative with 50 Gm. in 5 months	1 case of pallor, subnormal temperature; 1 case of erythema
Krombach, K.: Klin. Wchnschr. **7**: 1512, 1928	16	5-30 Gm.	Reversed, all but one	3 Herxheimer reactions
von Kiss, P.: Jahrb. f. Kinderh. **126**: 211, 1929	18	15-20 Gm.	7 of 18 reversed	Vomiting and diarrhea
Tuscherer, J.: Monatschr. f. Kinderh. **45**: 62, 1929	..	21 Gm.	Equal to arsphenamine and mercury	
Smeloff, N. S., and Karabekoff, K. I.: Venerol. i dermat. **7**: 3, 1930	22	4-40 Gm.	Not as favorable as arsphenamine	
Müller, E.: Arch. f. Kinderh. **91**: 108, 1930	62 infants	40-50 Gm.	Reversed, all but two	
Huber, H. G.: Med. Welt **4**: 1331, 1930	16 nurslings to 1¾ yrs.	22.5-30 Gm.	All reversed	1 case of transient pyuria; 1 of fever; 3 of transient diarrhea; morbilliform rash and fever
Huber, H. G.: Med. Welt **4**: 1331, 1930	7 from 1¾ to 10 yrs.	22.5-30 Gm.	1 reversed by 1 course; 2 received 2 courses without effect	6 cases of fever and rash (Jarisch-Herxheimer reaction); 2 of malaise
Bratusch-Marrain, A.: Arch. f. Kinderh. **92**: 26, 1930	47	0.01-0.02 Gm. per Kg. per day for 9 weeks	43% reverse vs. 29% reverse with neoarsphenamine and mercury	
Martin and Vierkotten: Monatschr. f. Geburtsh. u. Gynäk. **84**: 128, 1930	117	8 Gm.	5 cases remained negative 27 months	2 cases of paralysis with larger doses
Oppenheim, M.: Arch. f. Dermat. u. Syph. **160**: 200, 1930; Oppenheim, M., and Fessler, A.: ibid. **156**: 549, 1928	36	0.25 Gm. per Kg. total dose	Favorable	Diarrhea, fever, skin rash

47. Krösl, H.: Versuche und Erfahrungen mit Stovarsol und Spirocid, Wien. klin. Wchnschr. **37**:1209 (Nov. 20) 1924; Innerliche Verabreichung von Paraoxymetaazetylamidophenylarsinsäure bei Syphilis, Deutsche med. Wchnschr. **50**:1565 (Nov. 7) 1924; Weitere Erfahrungen mit Northovan und Spirocid, Arch. f. Dermat. u. Syph. **151**:299, 1926.

the patients received acetarsone alone, and in this case the Wassermann reaction became negative, while in the two cases receiving a combined treatment the Wassermann reaction remained positive. The following year Soldin and Lesser [48] reported seven cases, and noted that the drug was well borne by infants a few days old, and that the Wassermann reaction was favorably influenced in all cases. Since then, from European clinics, numerous reports have appeared, the most important of which are summarized in table 3. Scherber [49] and von Mettenheim [50] also reported favorable results with acetarsone in congenital syphilis.

It will be seen from table 3 that the dosage varies considerably. However, this variation is more apparent than real, for in general most investigators start with small doses, such as one-fourth tablet a day, and increase gradually to from one to four tablets a day, depending somewhat on the age and tolerance of the patient.

Tuscherer,[51] irrespective of the age of the patient, used the following regimen:

¼ tablet once a day for three days
¼ tablet twice a day for three days
¼ tablet three times a day for three days
¼ tablet four times a day for three days
½ tablet three times a day for three days
½ tablet four times a day for three days
1 tablet twice a day for three days
1 tablet three times a day for twenty days

Total: 84 tablets (21 Gm.) in forty-one days

After a six weeks' pause, a similar course was instituted regardless of the serologic reactions.

This method was, at first, generally used in our cases except when complications intervened.

From a review of the work of the authors mentioned, it is interesting to note that the drug may be administered successfully to new-born, premature and full term infants, even during the first few days of life. Some authors allow rest periods of varying lengths between courses of treatment, and others administer the drug continuously until the Wassermann reaction has been reversed. If treatment is inadequate, a

48. Soldin, M., and Lesser, F.: Stovarsol bei Säuglingssyphilis, Deutsche med. Wchnschr. **51**:991 (June 12) 1925.

49. Scherber, G.: Prophylaxe der Lues und Behandlung der hereditären Syphilis, Wien. klin. Wchnschr. **40**:909 (July 14) 1927.

50. von Mettenheim, H.: Ueber die perorale Behandlung der Lues congenita im Säuglingsalter mit Spirozid, Med. Klin. **27**:422 (March 20) 1931.

51. Tuscherer, J.: Zur Behandlung der Lues congenita mit Spirozid, Monatschr. f. Kinderh. **45**:62 (Sept.) 1929.

Wassermann reaction that has become negative may again become positive. For this reason Soldin and Lesser [52] administered as much acetarsone after the Wassermann reaction had become negative as was given before. This seems to us a reasonable procedure, and we have followed it in our work.

The effect on the Wassermann reaction is said to be favorable by all the writers. Von den Steinen [53] reversed eight of nine positive Wassermann reactions in from three to four months; Krombach [54] reversed all but one; von Kiss [55] seven of eighteen; Müller [56] sixty of sixty-two, and Huber [57] all in sixteen nurslings. Tuscherer [51] said that acetarsone is as effective as arsphenamine and mercury in reversing Wassermann reactions. Bratusch-Marrain [58] reported that of forty-seven patients with congenital syphilis treated with acetarsone, twenty (42.7 per cent) became seronegative; of fifty-one patients treated with neoarsphenamine and mercury, fifteen (29.4 per cent) became negative. Soldin and Lesser [52] reported that the reactions in seven cases became negative in two months with 15 Gm. of acetarsone; in two, in nine weeks with 20 Gm. of acetarsone; in three, in ten weeks with 25 Gm. of acetarsone, and in one, in five months with 50 Gm. of acetarsone.

Martin and Vierkotten [59] reported that five of their patients whose Wassermann reactions were reversed with treatment still gave negative reactions twenty-seven months after the last dose.

There is fairly uniform agreement that acetarsone is less effective in reversing Wassermann reactions in older children than in infants, and that in common with other methods of therapy, longer periods of treatment are necessary in older children than in infants. Some of the writers used bismuth, neoarsphenamine, arsphenamine or mercury or a combination of two or more of these with acetarsone in older children;

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52. Soldin, M., and Lesser, F.: Weitere Erfahrungen mit Spirozid, Deutsche med. Wchnschr. **54**:958 (June 8) 1928. Lesser, F.: Die interne Behandlung der Säuglingslues mit Spirocid (Stovarsol), Arch. f. Dermat. u. Syph. **160**:198, 1930.

53. von den Steinen, R.: Zur Behandlung der kindlichen Lues mit Spirozid, München. med. Wchnschr. **74**:1006 (June 17) 1927.

54. Krombach, K.: Beitrag zur Spirocid Behandlung der kongenitalen Säuglingslues, Klin. Wchnschr. **7**:1512 (Aug. 5) 1928.

55. von Kiss, P.: Der huetige Stand der peroralen Behandlung der Lues congenita, Jahrb. f. Kinderh. **126**:211, 1929.

56. Müller, E.: Die Spirozidbehandlung der angeborenen Syphilis und ihre bisherigen Erfolge, Arch. f. Kinderh. **91**:108 (July 25) 1930.

57. Huber, H. G.: Zwei Jahre Spirocidtherapie bei Lues congenita, Med. Welt **4**:1331 (Sept. 13) 1930.

58. Bratusch-Marrain, A.: Wert und Durchführung der Spirocidbehandlung der Syphilis im Kindersalter, Arch. f. Kinderh. **92**:26 (Nov. 28) 1930.

59. Martin and Vierkotten: Die angeborene Syphilis, Monatschr. f. Geburtsh. u. Gynäk. **84**:128, 1930.

some used acetarsone alone and some used other methods of treatment. However, in infants most of the writers used only acetarsone.

All reported favorable effects on the signs of syphilis; the clinical symptoms cleared up in from three to four weeks, and the skin cleared in from one to four weeks; the spleen and liver shrank to their original size in from four to eight weeks. Müller [57] stated that these changes are not as rapid as when patients are being treated with neoarsphenamine and mercury. Tuscherer [51] stated that the results are "in no way inferior" to those obtained by the generally employed injection treatment with arsphenamine and mercury.

The toxic effects noted are less varied than in adults and much less common in infants than in older children. Herxheimer reactions are rather commonly reported in children, but these are not severe; Klaften [60] considers them so mild that he does not interrupt treatment when they occur. A morbiliform skin rash occurs so commonly that it must be considered more than a coincidence; also, fever, diarrhea and vomiting must be considered as definite toxic symptoms. In nine of eighteen patients treated by von Mettenheim,[50] the stools became thin and mucoid. In five of these cases the drug was continued without difficulty. In two cases it was resumed after an interval of a few days, and in two cases the drug had to be discontinued. There is no mention of albuminuria except by one author,[61] who reported that in two of sixteen cases there were albuminuria and cylinduria. In one of these the albuminuria was present before the acetarsone therapy was begun; in the second, the albuminuria became worse when the acetarsone was stopped. In both cases the urine cleared up under acetarsone therapy. A third case showed transient pyuria for two weeks. Von Mettenheim [50] reported a case of syphilitic nephritis in which the patient recovered following acetarsone therapy.

The two cases of paralysis in infants in which large doses of acetarsone were given, previously noted, will be discussed in more detail subsequently. The death of two patients with lymphogranulomatosis and of one patient of our own with congenital syphilis are the only deaths reported as due to acetarsone.

There has been repeated comment on the excellent state of nutrition maintained by the infants being treated with acetarsone, and even more frequent comment on the lowered death rate under acetarsone therapy

60. Klaften, E.: Ueber Spirocidbehandlung der Neugeborenen, nebst weiteren Leitsätzen zur Präventivkur, Zentralbl. f. Gynäk. **51**:400 (Feb. 12) 1927; Die Grundlagen der antisyphilitischen Behandlung der Neugeborenen, Klin. Wchnschr. **7**:458 (March 4) 1928.

61. Martin, E.: Spirozidschäden bei Säuglingen, München. med. Wchnschr. **77**:936 (May 30) 1930.

than under the more orthodox arsphenamine therapy; however, tables 4 and 5 give the only statistics available actually comparing the results of the two methods of treatment.

Soldin and Lesser [52] reported their results before and after the advent of acetarsone therapy, as indicated in table 4.

It is to be noted that these series of cases do not run concurrently, and this permits the possibility that the results may have been influenced by other factors.

Huber,[57] comparing stovarsol with arsphenamine and bismuth or mercury in infants in parallel series, summarized his results as shown in table 5.

TABLE 4.—*Results of Soldin and Lesser*

	Before Acetarsone, 1919-1923	After Acetarsone, 1924-1927
Patients treated	47	46
Deaths	24	13
Percentage of deaths	51	28

TABLE 5.—*Results of Huber*

	Acetarsone	Arsphenamine and Mercury
Patients treated	16	16
Vomiting	0	4
Gain in weight (weekly)	120 Gm.	90 Gm.
Diarrhea	3	9
Deaths	2 (purulent bronchitis and erysipelas)	5 (bronchopneumonia, 4; bronchiolitis, 1)
Other infections	4 mild	9 persistent
Urinary manifestations	3 (pyuria, 1; albuminuria, 2)	4

The cases of albuminuria discussed previously occurred in this series and were not considered by Huber to be due to acetarsone.

DOSAGE OF ACETARSONE

The work in our clinics with acetarsone was begun very cautiously with a preliminary course of mercury or mercury along with acetarsone for a short time, but soon acetarsone therapy alone was used in the infants, and toward the last of our work the older children were given bismuth in the rest periods. The system of dosage followed was largely that of Tuscherer,[51] except when toxic symptoms intervened; then the dosage was lowered or the drug discontinued. Late in our work, because of the report by Martin [61] on two cases of paralysis occurring in infants treated by him and two cases of acetarsone poisoning in our

own work, to be discussed subsequently, it was decided to adopt the following schedule:

¼ tablet once a day for one week
¼ tablet twice a day for one week
¼ tablet three times a day for one week
¼ tablet four times a day for one week
½ tablet three times a day for one week
½ tablet four times a day for one week
1 tablet twice a day for one week

Total: 56 tablets (14 Gm.) in forty-nine days, followed by a six weeks' rest period

The foregoing total is two thirds of Tuscherer's total dosage over a period that is eight days longer. It is evident that the dosage of the drug must be governed by the tolerance of the patient treated toward it. In some cases it may be practical to use Tuscherer's method; in others, ours may prove more satisfactory, but there can be no hard and fast rule. The dangers of the drug are so evident that the child should be kept under close observation and should be seen at least once a week. Vomiting or diarrhea should be regarded as evidence of toxic symptoms and the drug temporarily discontinued, to be resumed again, even more cautiously, on disappearance of the symptoms.

DETAILED REPORT OF CASES

CASE 1.—The infant was born on Aug. 20, 1930. The result of the Wassermann test of the cord blood was 4+ to two antigens. The birth weight was 3,750 Gm. (8¼ pounds). The mother's Wassermann reaction was 4+ to two antigens prior to delivery as well as two months afterward. Immediately prior to pregnancy, the mother received six injections of neoarsphenamine and ten injections each of 1 grain (0.065 Gm.) of mercury salicylate. During pregnancy, the mother received nineteen injections of 0.060 Gm. of mercury salicylate, four doses of 0.4 Gm. of arsphenamine and one dose of 0.3 Gm. of arsphenamine and 1 ampule of bismuth. Treatment with acetarsone was begun on September 17, at about 1 month of age. Near the end of the course of 21 Gm. (October 22), reactions to the Wassermann test were 2+, 3+ and negative. The weight was 5,940 Gm. (13 pounds and 1 ounce), at the age of 2 months. On December 3, after a rest period, the Wassermann reaction was negative, when a second course of acetarsone was started; the weight was 7,240 Gm. (15 pounds and 14 ounces). Twenty-one grams of acetarsone was given, after which the Wassermann reaction was again negative, on Jan. 19, 1931; at the age of 5 months, the infant weighed 8.6 Kg. (19 pounds). On March 2, at the age of 6½ months, the weight was 9.3 Kg. (20 pounds and 8 ounces); a third course of 21 Gm. was started, and the Wassermann reaction was negative before and after the course (April 15). During the last two courses, the urine showed a positive test for albumin, but twenty-five days later, Heller's ring test gave negative results, and the heat and acetic acid test gave only a questionable clouding. The sediment was always normal.

CASE 2.—The infant was born on May 10, 1930. The cord blood gave a 4+ reaction. The mother had received two injections of 0.03 Gm. of mercury salicylate and one injection of bismuth. Her Wassermann reaction was 4+ a month

TABLE 6.—*Acetarsone Therapy in Infants Under One Year of Age**

						Treatment of Infant with Acetarsone				
Case	Age at Start of Treatment with Acetarsone	Serologic Reactions and Age	Mother's Serologic Reaction During Pregnancy	Mother's Treatment During Pregnancy	Preliminary Treatment of Infant	Total Dosage of First Course, Gm.	Serologic Reactions at End of First Course	Serologic Reactions at End of First Rest Period	Total Dosage of Second Course, Gm.	Serologic Reactions at End of Second Course
1†	1 mo.	4+; 4+ cord blood	4+; 4+	Good	None	21	2+; 4+	—; —	21	—; —
2	3½ mo.	4+; 4+ cord blood	4+; 4+	Poor	Mercury rubs, 36 days; serologic reactions thereafter negative	21	—; —	..	8.25	—; —
3	1 mo.	3+; 3+; 2+ 1 day	4+; 4+; 3+	None	Mercury by mouth and intramuscularly, 1 month	13.5	2+; ?	—; 1+	21	—; —; ..
4	6 wk.	3+; 4+ 10 days	4+; 4+; 4+	Good except last 3 months	Mercury by mouth, 6 weeks; Wassermann thereafter 1+; 3+	21	—; —; —	..	21	—; —; —
5	11 mo.	3+; 4+; 3+ 10 mo.	4+; 4+; 3+	None	Sulpharsphenamine, 0.05 Gm. twice; serologic reactions thereafter negative	19.5	—; —; —	..	..	..
6	3 mo.	—; — 3 mo.	3+; 3+	Poor	Mercury rubs, 30 days	21	..	..	8.25	—; —
7‡	7 days	3+; 3+ 5 days	4+; 4+; 4+	Good last 2 months	None	6	..	..	6	—; —; —
8	27 days	—; —; — 4 days	—; 3+; —	Good last 2 months	Mercury by mouth, 28 days	21	—; —; —	..	4	—; —; —
9	19 days	2+; 2+ cord blood	4+; 4+; 4+	Good	None	21	—; —			
10	6 wk.	1±; — cord blood	4+; 4+; 4+	None	None	21	—; 1±	—; —		

* In this paper, except where otherwise stated, serologic reactions are reported as follows: first, Wassermann reaction with alcoholic antigen; second, Wassermann reaction with cholesterolized antigen, and third, the Kahn reaction. For example, in case 3, the blood serum obtained at the age of 1 day was reported 3+ to the alcoholic and cholesterolized antigens of the Wassermann test and 2+ to the Kahn test.

† This patient was given a third course of 21 Gm. of acetarsone. The serologic reaction remained negative.

‡ This patient was given a third course of 13 Gm. of acetarsone. The serologic reactions remained negative.

before delivery. Mercury rubs were advised at the hospital for the infant. The physician caring for the infant thought that these were given irregularly. However, the Wassermann reaction was negative at 3 months of age. Two weeks later, acetarsone was started, December 10. The urine showed a trace of albumin irreg-

ularly before and during treatment. The sediment was repeatedly normal. The Wassermann reaction remained negative.

CASE 3.—The patient was born on June 18, 1930. The mother was not treated. Her reactions to Wassermann tests were 4+, 4+ and 3+. The placenta was normal. The patient's reactions to two Wassermann tests made on June 19 were both 3+; to the Kahn test, 2+. The infant received mercury intramuscularly and by mouth according to Jean's regimen for one month. Treatment with acetarsone was started on July 19, at the age of 1 month. Two reactions to the Wassermann test were 4+; the reaction to the Kahn test was negative. Thirteen and five-tenths grams was given over seven weeks. On September 6, the Wassermann reaction was 2+ to the alcoholic antigen and was unsatisfactory to cholesterolized antigen. A month's rest was given, and the Wassermann reaction remained positive. It is notable that this is the only infant requiring more than one course to reverse the Wassermann reaction, and this first course was but two-thirds the amount given later in our work. A second course of acetarsone was started on October 18, and 21 Gm. was given. The Wassermann and Kahn reactions were negative on March 14 and May 2, 1931, at the age of 10½ months. This patient developed nasopharyngitis, otitis media and mild diarrhea while under treatment, but these were not severe enough to interfere with the medication. The patient made a steady but slow gain in weight; he was always underdeveloped, but was always well nourished.

CASE 4.—The infant was born on Oct. 7, 1930. The mother was given six injections of 0.1 Gm. of bismuth and seven injections of from 0.2 to 0.3 Gm. of arsphenamine the first six calendar months of pregnancy. The last three months she was not treated. The placenta was suggestive but not diagnostic of syphilis. The mother's Wassermann reaction was 4+ to two antigens; the Kahn reaction was 4+ before delivery, and 4+, 4+ and 3+ after delivery. The patient had shining soles and palms and definite snuffles at birth. The snuffles were about two months in disappearing. The Wassermann reactions at ten days to two antigens were 3+ and 4+, respectively. A preliminary course of mercury was given for six weeks. The Wassermann reactions were negative and 3+ to two antigens, on November 7, at the age of 1 month. A course of acetarsone was started on November 22, and 21 Gm. was given. The Wassermann reaction to two antigens and the Kahn reaction were negative on Jan. 3, 1931. A rest period was given until February 14, followed by a second course of 21 Gm. On April 11, the Wassermann and Kahn reactions were negative, at the age of 6 months. This patient had nasopharyngitis with diarrhea during the course of treatment, but this was not severe enough to interfere with therapy. During the second course, the patient showed a very slight trace of albumin in the urine.

CASE 5.—The infant was born on April 9, 1930. The mother's Wassermann reaction was 4+ to two antigens; the Kahn reaction was 3+. The patient was first seen at 10 months of age, when she had bronchopneumonia, pertussis, acute nasopharyngitis and suppurative otitis media. The Wassermann reactions at this time were 3+, 4+ and 3+ (Feb. 9, 1931). The patient was transferred to another hospital later, and a Wassermann test made there on March 3 gave a 2+ reaction. Two intramuscular injections of 0.05 Gm. of sulpharsphenamine were given on March 3 and 10. The patient returned to the clinic on March 21, and the Wassermann and Kahn reactions were negative. Acetarsone was started and given regularly until two days before the end of the course, when nasopharyngitis, otitis media and diarrhea developed. Acetarsone was discontinued, the patient having received 19.5 Gm. in all. The infection of the upper respiratory tract cleared up

in about a week, and the diarrhea ceased at the same time. The Wassermann and Kahn reactions were negative on June 6, 1931, at the age of 14 months.

Case 6.—The infant was born on May, 13, 1930, following an automobile accident, after six and one-half months of gestation. The birth weight was 1,700 Gm. (3¾ pounds). The mother had had a 3+ Wassermann reaction to two antigens three times during the pregnancy. During the pregnancy she had received three injections of neoarsphenamine of 0.3 Gm. each and three intramuscular injections of mercury salicylate of 0.3 Gm. each. At 3 months of age, the infant had a negative Wassermann reaction, and he had had mercury rubs irregularly for a month. A 21 Gm. course of acetarsone was given. The urine was repeatedly negative. During the rest period, the patient developed an infection of the upper respiratory tract from which he made a good recovery. On December 4, at 6½ months of age, the Wassermann reaction was again negative, and a second course of 8.25 Gm. was given in twenty-five days, when bilateral purulent mastoiditis and bronchopneumonia developed. The patient died ten days after the cessation of the administration of acetarsone. Autopsy showed no evidence of injury by the drug. The urine was normal.

Case 7.—The patient was born on March 1, 1931. The Wassermann reaction at 5 days was 3+ to two antigens. The mother's Wassermann reaction was 4+ to two antigens; the Kahn reaction was 4+. The mother received eight injections of from 0.35 to 0.40 Gm. of sulpharsphenamine during the last two months of pregnancy. The placenta was normal. Acetarsone was started at 7 days, and 6 Gm. was given. A week's rest was given, and a similar course instituted. This was followed by a ten days' rest; the Wassermann and Kahn reactions of the blood on May 7 were negative, and a third course of 13 Gm. was begun. The Wassermann and Kahn reactions were negative on June 27, at the age of 4 months. The patient showed slight albuminuria before the first course of acetarsone was started, but this cleared up after two days of medication.

Case 8.—The infant was born on Aug. 31, 1930. Serologic reactions at 4 days of age were negative. The mother's Wassermann reactions were negative, 3+ and negative repeatedly. During the last two months of pregnancy, she was given seven injections of 0.3 Gm. of arsphenamine and one injection of 0.2 Gm. of arsphenamine. The placenta was normal. X-ray films of the infant's long bones at 6 days showed suggestive syphilitic periostitis. There were definite snuffles. The patient was given gray powder by mouth for six weeks, and from September 27 to November 15 was given a total of 21 Gm. of acetarsone. The Wassermann and Kahn reactions were negative on November 29, at the age of 3 months. A rest period was given, and a second course was started on December 27. After 4 Gm. had been taken, bronchopneumonia, otitis media and parenteral diarrhea developed. X-ray pictures of the long bones, taken on December 30, showed no evidence of periostitis. Medication was discontinued. The urine was normal. On April 21, 1931, another course of 4.12 Gm. of acetarsone was given. Nasopharyngitis with diarrhea developed, and the drug was discontinued. On May 16, a 4 Gm. course was begun. The Wassermann and Kahn reactions were negative on July 2, at the age of 9 months.

Case 9.—The birth weight of this infant was 3,400 Gm. (7 pounds and 9 ounces). The Wassermann reaction of the cord blood was reported 2+ to both the cholesterolized and the noncholesterolized antigens. Four years previously the mother of this child had delivered a macerated fetus after eight months' gestation. The fetus presented gross and microscopic lesions of syphilis, including spirochetes in the spleen. Her reactions at this time to the Wassermann tests were both 4+;

to the Kahn test, 4+. Two years later she delivered a normal child. She denied having had treatment during this interval, and did not believe that she had syphilis. There is no record of serologic reactions at the time of birth of this child, and the Wassermann and Kahn reactions of the child were reported negative at the time positive serologic reactions were demonstrated in the mother's serum when she entered the prenatal clinic at Genesee Hospital prior to the delivery of the infant to be discussed in case 10. For two and one-half months she received weekly injections of 0.40 Gm. of arsphenamine. Following this for nine weeks she received weekly injections of mercuric chloride, 0.066 Gm. The Wassermann and Kahn reactions at this time were all 4+. A week later the child under discussion was born. Because of the mother's history and the positive reaction in his own blood, the child was referred for treatment with acetarsone. This was started when the infant was 19 days old, and the outline of Tuscherer [51] was followed, except that the dosage was frequently reduced because of loose bowel movements. The infant's weight at this time was 3,700 Gm. (8 pounds and 2 ounces), and the Wassermann reactions of the blood were reported as 1+ and 2+ to two antigens. Over a period of sixty-six days he received eighty-four tablets, or 21 Gm. of acetarsone. His weight at the end of this time was 4,980 Gm. (10 pounds and 15 ounces), a gain of 1,280 Gm. (2 pounds and 13 ounces), and the Wassermann reaction of the blood was negative. The child is now receiving a six weeks' rest period.

CASE 10.—This patient weighed 4,040 Gm. (8 pounds and 14 ounces) at birth. The Wassermann reaction of the cord blood was 1± to the alcoholic antigen, and 1+ to the cholesterolized antigen. The mother had two living children, 9 and 4 years old, respectively. Two years before this baby was born she had a miscarriage, the etiology of which is unknown. Three months before the patient under discussion was born the mother's Wassermann reactions were reported as 4+ to two antigens, on two successive tests a week apart. She refused treatment, and because of her history and the positive reaction in the infant's cord blood, the child was referred for treatment with acetarsone at the age of 6 weeks. Her weight at this time was 5,000 Gm. (11 pounds), and the Wassermann reaction of the blood was reported as 1± to the noncholesterolized antigen, and 4+ to the cholesterolized antigen. The infant was normal on physical examination. She received a total of eighty-four tablets of acetarsone (21 Gm.) over a period of forty-one days. At the end of this time, she weighed 5,608 Gm. (12 pounds and 6 ounces), a gain of only 608 Gm. (1 pound and 6 ounces). She had presented somewhat of a feeding problem during this time, and only during the last two weeks of treatment were her gains very considerable. The Wassermann reaction of the blood at the end of the first course of treatment was negative to the noncholesterolized antigen and 1± to the cholesterolized antigen. The serologic reactions were negative after a six weeks' rest period, when the second course of treatment was started.

COMMENT

It is our opinion that the first five patients had syphilis. The last five may not have had syphilis, but in view of the great difficulty in determining which infants may have or may develop syphilis and the greater ease with which syphilis may be cured in the first few months of life, it has been the policy in our clinics to treat with mild antisyphilitic therapy all offspring of syphilitic mothers, starting very shortly after birth. During this period the mothers are more willing than

later to bring their infants to clinics, because they are seeking advice on feeding and the general care of the infant. Hence, the infants in our series would have been treated by Jean's regimen of arsphenamine and mercury if they had not been treated with acetarsone.

Von Mettenheim [51] has observed, as have many others, that in recent years the picture of congenital syphilis has changed, owing to the more active treatment of syphilitic mothers during pregnancy, so that many children are born without clinical manifestations of syphilis and are only slightly infected. For this reason, in such cases less drastic means of treatment than intravenous and intramuscular injections may be effective and therefore justified. Hence, although satisfied with the results of the older methods of treatment, von Mettenheim now treats patients with congenital syphilis with acetarsone.

TABLE 7.—*Effect of Treatment of Pregnant Women on the Incidence of Syphilis in the Offspring*

Author	Number of Cases	Treatment of Mother	Percentage of Syphilitic Children
Williams	169	None	48.5
	102	2 to 3 injections of arsphenamine	33.2
	178	One course of 4 to 6 injections of arsphenamine and mercury	6.7
Beck	11	1 to 3 injections of arsphenamine	54.0
	17	5 or more injections of arsphenamine	6.0
Boas and Gammeltoft	158	None	99.0
	111	Mercury only	71.0
	79	Arsphenamine	24.0
Galliot	144	Neoarsphenamine	8.0
Bodin	28	Neoarsphenamine	7.0

Just how soon after birth a case can be diagnosed syphilis, unless physical signs are unmistakable, is open to debate. The probability that a patient may have had syphilis can be roughly estimated from the following data: Williams [62] found that 76 per cent of the infants with positive Wassermann reactions of the cord blood were later shown to have syphilis. Jeans and Cooke [63] stated that if the Wassermann reaction is 4+ on the cord blood, the patient only rarely is not syphilitic, 97.6 per cent being syphilitic in their series. To reason from another angle, Jeans and Cooke (quoted by Stokes [64]) have found that if the mother's Wassermann reaction is strongly positive, over 70 per cent

62. Williams, J. W.: The Value of the Wassermann Reaction in Obstetrics: Based upon the Study of 4547 Consecutive Cases, Bull. Johns Hopkins Hosp. **31**:336 (Oct.) 1920.

63. Jeans, P. C., and Cooke, I. V.: A Study of the Incidence of Hereditary Syphilis, Am. J. Dis. Child. **22**:402 (Oct.) 1921.

64. Stokes, J. H.: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1926, p. 1013.

of the infants will have syphilis. Of those infants who later were shown to have syphilis, the same authors found that 45 per cent had a strongly positive Wassermann reaction at birth. Eighteen per cent had a weakly positive Wassermann reaction, and 37 per cent had negative Wassermann reactions. Stokes [65] quoted the authors given in table 7 to show the effect of treatment of pregnant women on the incidence of syphilis in the offspring.

Although there may be some question as to the significance of the early Wassermann reaction in these infants, we think that it is extremely important that they were all negative after a short course of treatment and have stayed negative in the age period when the Wassermann

TABLE 8.—*Results in Four Hundred and One Infants Under One Year of Age*

Received One Course or Less			Treated Six Months or More		
	Number	Per Cent		Number	Per Cent
Recovered	9	3	Cured 3 years (20 neurosyphilis)	90	72
Died	99	36	Not serologically cured (12 neurosyphilis)	35	28
Lost	168	61			
Total	276			125	

TABLE 9.—*Results in Five Hundred and Forty-Two Patients Over One Year of Age*

One Course or Less			Treated from Six Months to One Year			Treated More Than One Year		
	No.	Per Cent		No.	Per Cent		No.	Per Cent
Recovered	9	3	Cured (1 neurosyphilis)	8	12	Cured (14 neurosyphilis)	85	44
Died	11	4	Not serologically cured (7 neurosyphilis)	58	88	Not serologically cured (20 neurosyphilis)	108	66
Lost	263	93						
Total	283			66			193	

reaction is more significant than at any other time in life. It is notable also that in every case the nutrition was well maintained, and except for albuminuria that cleared up and occasional loose bowel movements and vomiting, no toxic symptoms were noted that could not be explained otherwise.

Furthermore, the parents were the most faithful parents we had in bringing their children to the clinic. As they realized the discomfort of needle therapy, they were anxious to have their children treated by mouth. We have been embarrassed by parents demanding that we use acetarsone in treating their children. We have had considerable difficulty in keeping up the attendance of children and infants being treated in the routine arsphenamine-mercury manner. Parents, seeing no evi-

65. Stokes (footnote 64, p. 1056).

dence of syphilis in their children, do not like to bring them to the clinic for painful treatments. This is brought out by Jeans and Cooke,[66] who reported their results as shown in table 8.

Their work also brings out the importance of treating in the first few months of life (table 9).

One course consisted of three injections of arsphenamine and three injections of mercuric chloride given concurrently at weekly intervals; this was followed by six weeks of mercury by mouth with weekly injections of corrosive mercuric chloride.[67]

The higher death rate under the mercury-arsphenamine regimen has been frequently commented on by European writers. Treatment, to be effective, very often is too severe for the patient. The advocates of acetarsone think that they have now a method of treatment that is less rigorous than the standard arsphenamine-mercury treatment, but nevertheless effective in infants.

It was for the purpose of ascertaining the facts concerning this that our work was started.

TOXIC NEUROLOGIC SYMPTOMS AS A RESULT OF ACETARSONE THERAPY

The cases to be described were not included in table 6, because in the first it was necessary to discontinue acetarsone therapy before completion of the first course of treatment on account of development of alarming toxic symptoms, and in the second case, although the serologic reactions were reversed, the patient died, probably as a result of the therapy.

CASE 1.—The mother of F. M., an Italian woman, aged 40, had had a miscarriage at 7 months, twenty years previously. There had been no intervening pregnancies. Her reactions to two Wassermann tests (as well as those of her husband) were both 4+ at the beginning of this pregnancy. At this time she received 0.4 Gm. of neoarsphenamine intravenously, and a week later 0.60 Gm. Following the second injection she became severely ill, the chief symptoms being vomiting and jaundice. Because of this, arsenic therapy was discontinued, and at regular intervals, until the end of her pregnancy, she was treated rather vigorously with various bismuth preparations.

Despite the foregoing therapy, the Wassermann reaction of the cord blood when the infant was born was 4+ to two antigens; the Kahn reaction was negative; the reactions were the same on the infant's blood at the age of 20 days, when he was first referred for treatment. At this time he weighed about 3,860 Gm. (8½ pounds) and appeared normal in every respect, except that there was a scar at the base of the right thumb where a small supernumerary digit had been removed.

The infant was given acetarsone according to the dosage and method recommended by Tuscherer.[51] He took the drug well and gained steadily in weight until he reached a dosage of 0.25 Gm. three times a day, when he began to vomit.

66. Jeans, P. C., and Cooke, I. V.: Prepubescent Syphilis, New York, D. Appleton & Company, 1930, p. 2823.

67. Jeans, P. C.: Personal communication to the authors.

For this reason the dosage was reduced to 0.125 Gm. of acetarsone four times a day. At the age of 6 weeks he had taken twenty-six tablets, or 6.5 Gm. of the drug. The dosage was then increased to 0.25 Gm. in the morning and 0.125 Gm. three times during the remainder of the day. During the following week his bowels became quite loose, and when he was seen a week later, marked diarrhea had developed. At that time the child had taken thirty tablets, or 7.5 Gm. of the drug, and his weight was 4,800 Gm. (10 pounds and 9 ounces). The urine was normal. On examination at this time, it was noted that the child would occasionally show a marked opisthotonos. The anterior fontanel was flat; knee reflexes were present and not exaggerated, and the Kernig sign was not present. However, because of the diarrhea and the occasional opisthotonos it was thought best to discontinue the acetarsone for the time being. The Wassermann reactions of the blood serum of two antigens were 1+ and 3+ at that time; the Kahn reaction was negative, a remarkable change over a period of thirty-three days.

Five days after stopping treatment, when the infant was 8 weeks old, the father reported that the child seemed to have lost his voice. On examination at this time, the child weighed 4,950 Gm. (10 pounds and 9 ounces). The bowels were now normal. The urine at this time was normal. His voice was distinctly weakened and sounded more like a whisper than a cry. There was no stridor. Occasional opisthotonos was present, as seen previously. Chvostek and Trousseau signs were not present. The mother stated also that at times the child held his hands in a position resembling, from her description, that of the carpal spasm of tetany. It was thought, however, that because the child had received since the age of 1 month adequate doses of a standard brand of cod liver oil and had been fed only breast milk, he was probably developing toxic symptoms as a result of the acetarsone therapy, though tetany and possibly the late results of a cerebral birth injury had to be considered.

The following day the child was seen in consultation with Dr. S. W. Clausen, who made the following notation: "Baby shows slight general flaccidity but no evidence of paralysis. The voice is notably weak. Chvostek negative. The knee jerks are active and equal. There is occasionally slight tonic spasm of the muscles of the arm, especially the left, with inward rotation of the arm and flexion of the fingers. The impression is (1) possibly toxic effect of acetarsone, (2) tetany, and (3) organic disease of the central nervous system, luetic or due to some cerebral accident. This is, however, improbable."

A determination of the blood calcium at this time was reported as 11.3 mg. per hundred cubic centimeters, thus excluding tetany. Calcium thiosulphate, 0.25 cc. of a 10 per cent solution, was given intravenously for two successive days and then discontinued because of the difficulty of administration. Sodium thiosulphate, 0.03 Gm. (2 grains), was given by mouth every four hours. The infant is now making a slow but steady recovery.

CASE 2.—The family history in this case is not completely known. The mother had two miscarriages previous to the birth of this child, C. M., at which time the Wassermann reactions to the two antigens were both 4+, as was the Kahn reaction. There were no clinical signs of syphilis in the infant, except possibly some indistinctness in the epiphyseal lines of the right ulna on the roentgenogram. Acetarsone therapy according to the method of Tuscherer [51] was started when the infant was 29 days old. Her weight at that time was 3,680 Gm. (8 pounds and 1 ounce). The Wassermann reaction was 4+ to two antigens; the Kahn reaction was negative. Twenty-three days later, her weight was 3,900 Gm. (8 pounds and 9 ounces), and it was noted that the infant occasionally vomited following medica-

tion. However, as she looked well, although gaining poorly, the drug was continued. The following week she gained 230 Gm. (7 ounces) and seemed to be doing exceptionally well. The following day, however, at the age of 60 days, marked diarrhea developed. The day afterward the mother noted weakness of the extremities, and the child seemed disinclined to move. The next day the child was brought to the hospital. At this time the outstanding feature was a marked flaccidity of the extremities. They were moved occasionally spontaneously, and reacted to painful stimuli, but tendon reflexes could not be elicited. There were a slight stiffness of the neck and a tendency to opisthotonos when the child was placed on her side. The outstanding feature was the marked flaccidity. This was such that if arsenic poisoning had not been suspected because of the therapy the child was receiving, myatonia congenita (Opphenheim's disease) might have been considered.

Up until the time of admission the child had received thirty and three-fourths tablets, or 7.68 Gm., of acetarsone over a period of thirty-four days, and the Wassermann reaction was negative.

Spinal puncture demonstrated a normal cerebrospinal fluid, with a negative colloidal gold curve. The urine was normal; the hemoglobin was 75 per cent by

TABLE 10.—*Comparison of Results of Martin with Those in Two Cases Reported*

	Age in Days at Beginning of Treatment	Duration of Treatment in Days When Toxic Symptoms Developed	Nature of Toxic Symptoms	Acetarsone Given Before Toxic Symptoms Developed, Gm.
Martin's case 1.....	3	19	Flaccidity; stridor	16.5
Martin's case 2.....	16	22	Flaccidity	16.9
Authors' case F. M.....	20	33	Diarrhea; opisthotonos; flaccidity	7.5
Authors' case C. M.....	29	31	Diarrhea; flaccidity	7.68

the Sahli method, and the red cell count was 3,310,000 per cubic millimeter. The icterus index of the blood was 22 (definitely above normal); the blood calcium was 10.9 mg., and phosphorus, 4.8 mg. per hundred cubic centimeters. A stool culture was negative for B. typhosus, B. paratyphosus, A and B and B. dysenteriae.

The day following admission the child was given 0.25 cc. of a 10 per cent solution of sodium thiosulphate intravenously, and she died rather suddenly an hour and a half later. As sodium thiosulphate, particularly in such small doses, is generally regarded as nontoxic, we are inclined to attribute this infant's death to acetarsone intoxication.

A complete autopsy was made, including examination of the brain, spinal cord and peripheral nerves, but nothing abnormal was noted on gross examination. We hope to report in detail on the microscopic observations in this case at a later date.

As has been stated, Martin [61] reported two cases of flaccid paralysis developing after acetarsone therapy. For the sake of convenience in comparison his cases are tabulated, together with our own, in table 10.

It is notable that in Martin's cases the flaccidity was not at first attributed to the acetarsone and the drug was continued after the appearance of the first symptoms, so that the patient in case 1, at the

age of 36 days, had taken a total of 30 Gm. and the one in case 2 at the age of 65 days, had taken 24 Gm. of the drug, when treatment was stopped. The patient in case 1, at the age of 3 months, had flaccid paralysis of the legs, and the one in case 2, at the age of 2½ months, had spastic paralysis of the legs.

TABLE 11.—*Acetarsone Therapy in Children Over One Year of Age*

Case	Age in Yr.	Pathologic Findings	Serologic Reactions at Beginning of Treatment	Total Dosage of Acetarsone, First Course, Gm.	Serologic Reactions After First Course	Interval Treatment	Serologic Reactions Before Second Course	Total Dosage of Acetarsone, Second Course, Gm.	Serologic Reactions After Second Course
1*	7	Malnutrition; mulberry molar; irritability; unsteady gait	4+; 4+; 4+;	21	4+; 4+; —	None	4+; 4+; —	21	4+; 4+; 1±
2	4½	Headaches; irritability; pains in legs and joints; tires easily	4+; 4+; 2+	21	4+; 4+; 2+	None	..	8	4+; 4+; 3+
3	7	Interstitial keratitis; always tired and weak	4+; 4+; 4+	21	..	10 injections of 0.1 Gm. of bismuth intramuscularly	4+; 4+; 4+	21	4+; 4+; 3+
4	4	Malnutrition	4+; 4+; 2+	22.125	..	5 injections of 0.1 Gm. of bismuth intramuscularly	4+; 4+; 4+	21	4+; 4+; 4+
5	10	Slight malnutrition	3+; 3+; 4+	7.5	..	10 injections of 0.1 Gm. of bismuth intramuscularly	4+; 4+; 4+		
6	1¼	Underdevelopment; malnutrition	4+; 4+	21	4+; 4+; 3+	None	4+; 4+; 4+		
7	2	None	4+; 4+; 3+	21	4+; 4+; 4+	None	4+; 4+; 4+		
8	10	Malnutrition	3+; 4+; 1+	21	3+; 4+; 1+				
9	8	Malnutrition	4+; 4+; 3+	21	4+; 4+; 3+				

* After the second course of acetarsone, which consisted of five weekly intramuscular injections of 0.1 Gm. of bismuth, the Wassermann reaction was 4+; 4+; the Kahn reaction 1±. After another course of 21 Gm. of acetarsone, the Wassermann reaction became 3+; 4+; the Kahn reaction, negative.

Martin concluded that his two cases were undoubtedly due to acetarsone poisoning. He recommended that if the course of treatment is started directly after birth the total dosage should not exceed 9 or 10 Gm. It is interesting that our patients developed symptoms after taking even less than this amount of acetarsone.

Apparently the lesson to be learned from the four cases in table 10 is that acetarsone therapy in infants may be a highly hazardous pro-

cedure, much more so than the great majority of reports from foreign clinics would lead one to suppose. Many more cases must be studied under carefully controlled clinical conditions, and the dangers of acetarsone and how to avoid them, if possible, must be thoroughly understood before the drug may be recommended for general use.

CHILDREN OVER ONE YEAR OF AGE

As can be seen from the tables from Jeans and Cooke, quoted previously, the treatment for syphilis in older children requires longer than that in infants. Our work has continued for too short a time to permit any conclusions concerning the use of acetarsone in older children, but for the sake of completeness, our work is reported. It seems probable that acetarsone alone should not be relied on in the treatment for congenital syphilis in older children, but should be combined with bismuth, mercury or both. In the early work, we gave a preliminary course of mercury, but later we used bismuth and acetarsone only. All cases were definitely syphilitic. Table 11 summarizes the cases.

DETAILED REPORT OF CASES

CASE 1.—The patient was 7 years of age. The Wassermann reaction was 4+ to three tests. The spinal fluid was normal. The patient was malnourished, had a mulberry first molar tooth and was said to be nervous and irritable by her foster parents. She had a peculiar unsteady, somewhat propulsive gait and was difficult to manage at home and at school. She was given a seven weeks' preliminary treatment with mercury by mouth and by intramuscular injection. Then two courses of 21 Gm. each of acetarsone were given with an appropriate rest period between. The Kahn reaction became negative, and the Wassermann reaction remained 4+ to two antigens. The patient had gained 15 per cent over her weight before treatment began six and one-half months before. The gait was now normal, and the irritability was so improved and the child so much easier to manage that the school teacher and foster parents were much pleased. Five injections of 0.1 Gm. of bismuth were given intramuscularly. The Wassermann reaction was 4+ to two antigens; the Kahn reaction was 1±. Acetarsone was started again on May 2, and a course of 21 Gm. was given. The Wassermann reactions were 3+ and 4+ to two antigens; the Kahn reaction was negative.

During the first course of acetarsone, the girl complained of severe abdominal pain for two days. The parents were advised by telephone to diminish the daily dose of acetarsone one fourth for two days; then the patient was seen in the clinic and was found to have nasopharyngitis. Abdominal examination and urinary examination gave negative results. The acetarsone was increased to the usual dose and later was still further increased, and no untoward symptoms were noted.

During the second course of acetarsone, the patient showed a slight trace of albumin at times. In one twenty-four hour specimen of urine the amount was too small to measure by the Esbach method. By a modified Addis count, the red cells in the total twenty-four hour specimen of urine were 900,000, and the white blood cells, 10,000,000. As this was not catheterized urine, the white count must be disregarded. There are no standards for this method of doing an Addis count on children without limiting the intake of fluid. Some tests done in this hospital on

children would lead us to think that this count did not indicate any gross lesion in the kidneys. The albumin disappeared, and the sediment became normal after the acetarsone was discontinued. During the third course, the urine was normal repeatedly.

CASE 2.—A girl, aged 4½ years, had a Wassermann reaction of 4+ to two antigens; the Kahn reaction was 2+. Except for one intramuscular treatment a year before, the patient had had no antisyphilitic therapy. She had never been a strong child; she was irritable, difficult to control, cried easily and complained of headaches very frequently and always felt tired. She had complained of pains and "cramps" in the joints, but never any swelling. There were no pains in the long bones except near the joints. She was given one course of 21 Gm. of acetarsone, and her mother stated that all the symptoms mentioned were gone and that the child was "like a different girl." After the first course, the Wassermann reaction was 4+ to two antigens, and the Kahn reaction was 3+. After a six weeks' rest, the patient was given 8 Gm. more of acetarsone, when follicular tonsillitis developed and the therapy was interrupted. The patient is now (June 29, 1931) on the third course of acetarsone. The Wassermann reaction on June 29 was 4+ to two antigens, and the Kahn reaction was 3+.

CASE 3.—A boy, aged 7 years, had a Wassermann reaction of 4+ to two antigens; the Kahn reaction was also 4+. The patient came in because of severe interstitial keratitis of two weeks' duration. He had complained of feeling tired and weak for a year. He had not been treated for syphilis, except three years previously, when he had had a five weeks' course of mercury. He was now given a six weeks' course of acetarsone (21 Gm. total). By the end of the first week, he said that his eyes were definitely less painful, and he made a slow but definite improvement while on acetarsone, a much more rapid improvement than during the ten weeks thereafter when he received weekly injections of 0.1 Gm. bismuth. The Wassermann reaction at the close of the bismuth series was 4+ to two antigens, and the Kahn reaction was also 4+. He was given a second course of acetarsone (21 Gm.), and again there was a rapid improvement in the interstitial keratitis. On one visit the urine showed a few hyaline casts; since then it had been repeatedly normal. The Wassermann reaction at the close of the course was still 4+ to two antigens, and the Kahn reaction was 4+.

CASE 4.—The patient, aged 4 years, was a member of a syphilitic family. The Wassermann reaction was 4+ to two antigens; the Kahn reaction was 2+. The patient was malnourished. The patient was given 22 Gm. of acetarsone, followed by five injections of 0.1 Gm. of bismuth, after which the Wassermann reaction was 4+ to two antigens, and the Kahn reaction was also 4+. A second course of acetarsone was given after a rest period. On June 22, 1931, the Wassermann reaction was still 4+ to two antigens, and the Kahn reaction was still 4+.

CASE 5.—A boy, aged 10 years, the brother of the patient in case 4, had a Wassermann reaction of 3+, 3+ and 4+. He had received six weeks' treatment by intramuscular injection and by mouth, of mercury, four years before. There had been no therapy since for syphilis, until acetarsone treatment with 7.5 Gm. was given. When about 6.5 Gm. had been given, the patient went to bed with malaise, conjunctivitis and a measles-like rash. Two weeks later, he was seen in the clinic and had at that time a morbiliform rash over most of the torso. The rash was very dark, and there was a fine branny desquamation over some of the areas. There was still a slight injection of the conjunctiva. There was definite albuminuria, but there were no formed elements in the sediment. The albuminuria cleared slowly over a period of four weeks. The patient was given bismuth intra-

muscularly, and later mercury and arsphenamine. When placed on arsphenamine therapy, a mild pruritus developed that cleared up when the arsphenamine was discontinued. The Wassermann reaction was 4+ to two antigens; the Kahn reaction was also 4+.

CASE 6.—A girl, aged 15 months, had a Wassermann reaction of 4+ to two antigens. She was given 21 Gm. of acetarsone in ninety-seven days. A week before the end of the course, a trace of albumin appeared in the urine. This was present at the end of the course, but three weeks later the urine was normal. The patient had otitis media toward the beginning of the course, but medication was not interrupted. The weight at the beginning of the course was 8.1 Kg. (17 pounds and 12 ounces). The patient was small for her age, and her musculature was flabby. At the end of the course, she weighed 8.8 Kg. (19 pounds and 8 ounces). The Wassermann reaction at the end of the course was 4+ to two antigens; the Kahn reaction was 3+. At the end of six weeks, the serologic reactions were unchanged.

CASE 7.—This patient, aged 2 years, was the brother of the one in case 6. The Wassermann reaction was 4+ to two antigens; the Kahn reaction was also 4+. Twenty-one grams of acetarsone was given in forty-two days. The Wassermann and Kahn reactions remained the same. After thirty-four days of treatment, the urine showed 1+ albumin, but there were no organized elements in the sediment. The urine was normal one week after completion of the course; the Wassermann and Kahn reactions remained the same. At the end of six weeks the serologic reactions were unchanged.

CASE 8.—Physical examination of the patient, aged 10, disclosed nothing remarkable except moderate malnutrition. The Wassermann reactions were 3+ and 4+; the Kahn reaction was 1+. Twenty-one grams of acetarsone was given in forty-two days, and the Wassermann and Kahn reactions thereafter were the same.

CASE 9.—This patient, aged 8 years, was the brother of the patient in case 8. Physical examination revealed only moderate malnutrition. The Wassermann reaction was 4+ to two antigens; the Kahn reaction was 3+. Twenty-one grams of acetarsone was given over a period of forty-two days. The urine showed a slight trace of albumin on the thirty-fifth day, but it was normal a week after the completion of the course. The Wassermann and Kahn reactions remained the same.

The urine of all these children was repeatedly negative, unless otherwise stated.

Acetarsone was given to two other syphilitic children, aged 9 and 13 years, for a short time without any untoward effects. These patients were then transferred to a clinic closer to their home.

SUMMARY

Infants Under One Year of Age.—1. Acetarsone was given to twelve infants, syphilitic or the offspring of syphilitic mothers.

2. In the case of one infant, a flaccid paralysis developed from which a gradual recovery is now being made. In another infant flaccid paralysis developed, and death occurred, in our opinion, as the result of acetarsone therapy. Both of these infants had positive serologic reactions at the start of acetarsone therapy; these reactions reversed during the course of the therapy. These cases are discussed in detail.

3. Ten infants completed full courses of treatment.

4. Four Wassermann reactions that were negative at the start of treatment remained negative at 3, 5, 7 and 13 months of age, respectively.

5. Six Wassermann reactions that were positive at the start of acetarsone therapy were reversed. In three cases this occurred at the end of the first course of treatment; in two cases, at the end of the first rest period, and in another case, at the end of the second course of acetarsone therapy. In four of these cases the Wassermann reactions were negative at 2, 3, 5 and 6 months of age, respectively, and repeated Wassermann tests were negative at 4, 6, 8 and 11 months, respectively. Repeated Wassermann tests have not yet been done in the two remaining cases. Two of these six patients received mercury in small amounts preceding acetarsone therapy.

6. Definite physical signs of syphilis were present in only two cases, and these signs regressed rapidly and disappeared.

7. No new signs of syphilis developed.

8. The nutrition remained satisfactory in every case, or, if unsatisfactory at the start, showed marked improvement. This may in part have been due to the constant supervision these infants received incident to their treatment.

9. The mild toxic symptoms noted were transient albuminuria, mild diarrhea and vomiting. In some of the cases, the symptoms may have been due to coincident infections of the upper respiratory tract or otitis media.

10. From the report of Martin [61] of two cases and our experience in two cases, it is evident that the drug may have a highly toxic action on the central nervous system. Patients receiving acetarsone should be watched with extreme care, and the drug should be discontinued, at least temporarily, at the first sign of toxic symptoms.

Children Over One Year of Age.—1. Acetarsone was used in nine children from 1¼ to 10 years of age with congenital syphilis, but for insufficient time to permit any conclusions (from two to eight months). However, it seems rather definite that in common with other methods of treatment, the Wassermann reaction is not so easily influenced as in infants under 1 year of age.

2. One patient showed a morbilliform rash, conjunctivitis, malaise, apathy and albuminuria. The albuminuria required four weeks to clear up. Four patients showed transient albuminuria for a short period. One of them had a few red cells in the urine during the period of albuminuria, and at one time had abdominal pain for two days. One patient had a few hyaline casts in the urine at one visit only.

3. The parents of five of these children volunteered the information that the patients showed improvement in appetite, general vigor and

energy. We observed, in addition, improvement in the general health of three others.

4. One boy with acute interstitial keratitis showed marked improvement.

CONCLUSIONS

Acetarsone probably has a definite place in the treatment for congenital syphilis. That the drug cannot be used indiscriminately, as the reports from some foreign clinics might be interpreted to suggest, is amply demonstrated by the one fatality and the toxic manifestations that occurred in our small series. The advantages of the peroral treatment for congenital syphilis over the methods usually employed are evident. However, the exact position that acetarsone should occupy in the treatment for congenital syphilis, at least as far as this country is concerned, remains yet to be determined by those who have at their disposal sufficient clinical material for the study this drug deserves, and sufficient interest to follow their cases carefully so that there will be a minimum of danger to the patients concerned.

PSYCHIC ENURESIS IN NORMAL CHILDREN

AN EXPERIMENTAL STUDY

J. M. LEWIS, M.D.
AND
J. OSTROFF, M.D.
NEW YORK

It would seem superfluous to stress the importance of psychic factors in the causation of enuresis in children. The significance of these factors has been realized for many years and has been emphasized by all who have studied the subject. Only recently this aspect was fully considered by Anderson,[1] who reviewed the literature in an exhaustive and admirable manner. The object of the present paper is not to call attention to the psychic factor, but rather to show that this factor is capable of experimental study; in other words, that it can to a large extent be controlled and regulated at will. As far as we are aware, no study of this kind has been reported. It seemed that if a technic of this nature could be established, it would render possible an accurate study of this disturbing disorder and, incidentally, an appraisal of the many pharmacologic and therapeutic agents that are recommended for its cure.

This study was carried out in a model institution for child care which harbors children up to 4 years of age, thus affording opportunity for a long period of observation of the physical and mental status both previous and subsequent to our test. The children are kept in a main building which has large, light and well ventilated dormitories as well as in smaller buildings which are equipped with individual glass cubicles.

Enuresis has been and is an important problem in this institution, a fact that was brought out strikingly at the beginning of the study when we were able to find only eight children among forty, from 3 to 4 years of age, who did not wet themselves by day or by night. These eight children, seven of whom were boys, were carefully observed in the dormitories during a preliminary period of two weeks so as to be certain that they were absolutely and at all times continent. Some of them were among the brightest in the institution, and as a whole the group may be considered representative of this age period. Before

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1. Anderson, F. N.: The Psychiatric Aspects of Enuresis, Am. J. Dis. Child. **40**:591 (Sept.) 1930.

this study was begun these children were carefully examined physically to be certain that they had no organic defects.

Four of the children were transferred from the main building to one of the small buildings, which is divided into fourteen individual glass cubicles. They were confined to their cubicles during the twenty-four hour period for an entire week, and the day and night nurses were instructed to be on the alert for enuresis. The toilet facilities are the same as those in the main building, and no deviation in the toilet schedule was made.

The results of this change of quarters were striking. Within twenty-four hours after transfer to the small cubicles, enuresis developed in all these children, not only nocturnally but diurnally. In three, this incontinence lasted for only two days, whereas in one there was involuntary urination during the entire period of observation, namely, one week. It seemed of interest to ascertain whether this child would remain incontinent on transfer to the large dormitory in which he had been housed previously. Accordingly, he was sent back and observed for a period of two weeks. Except for the first night following transfer, he remained continent. As was to be expected, the other children remained continent when transferred to their original wards.

The possibility that the development of enuresis in these children was due largely to suggestion had to be considered as, to some extent, their attention was directed to bed-wetting. It was decided, therefore, to carry out a similar test in the course of which no mention whatsoever of enuresis should be made by either nurses or physicians. At the same time, in order to eliminate the factor of confinement and of isolation during the day, the children were to be allowed to play with others in the corridor and on the porch. Four new children were selected for this test; they were not transferred from the large dormitory until after supper and were immediately put to bed. The entire group of children became incontinent on the very first night following the change in surroundings. In three, enuresis persisted throughout the entire period of observation in the cubicle building, whereas one child adjusted himself to the change on the third day. As in the first group, enuresis occurred not only at night but also during the day. It should be mentioned that after the first twenty-four hours these children appeared to be happy in their new quarters, so that unhappiness cannot be considered as being responsible for the development of enuresis.

It was evident that enuresis was induced in these children as the result of transfer from large dormitories to small glass cubicles. The question arose as to whether a change in surroundings of lesser degree would have the same effect. It was therefore decided to transfer the four children of the second group to another large dormitory in the main building, and to observe them for one week. No incontinence of urine

was observed in any of the children during this period. In view of what has been suggested, it is of interest to record that one child remained continent although he was very unhappy during the first day, crying at times for his former nurse and remaining awake until a very late hour—another indication that unhappiness did not play a significant rôle in the causation of enuresis in this study.

To determine whether a second transfer from the large dormitories would have the same effect, two children of the second group were again transferred to the small cubicles for one week. Interestingly enough one child did not develop enuresis, and the other had incontinence but once during the entire period. This difference in reaction is explained obviously by the fact that the change in surroundings was no longer new and therefore did not result in psychic disturbance. The effect of confining these children throughout the day to their cubicles was then tried. No incontinence occurred, even though their attention was directed to bed-wetting during the last few days of observation. This test corroborates the deduction that neither confinement nor suggestion was the dominant factor in the causation of enuresis.

We believe that enuresis was induced in these children by the psychic effect of a strange and new environment, and that in some children psychic adjustment took place within forty-eight hours. This interpretation is borne out by the fact that when the change in surroundings was not marked, as for example, when they were transferred to a similar ward, incontinence did not result, and that if the change in environment had been previously made a second transfer resulted in a less degree of incontinence.

In this connection we should like to call attention to the development of enuresis in some children when they were transferred to private homes. It has likewise been our experience that the development of enuresis in these children was of temporary nature, and we ascribed it to change of environment.

It was of interest to make a test of the effect of tincture of belladonna under experimental conditions, as this drug is prescribed commonly for children suffering from this disorder. An opportunity was thus afforded to compare the effect of this drug with that of psychotherapy. Two of the children transferred to the cubicles were given belladonna. In spite of large daily doses, they continued to wet themselves; on the other hand, on transfer to the large dormitory, enuresis promptly ceased.

Enuresis must be regarded as a disorder that can be induced at will in some normal children and is thus open to experimental investigation. This permits a clinical test of various factors that have been considered causative of the disorder. It should be added, however, that a study of this kind can probably be successfully carried out only on young children

who have recently ceased to wet themselves, and that in somewhat older children, in whom continence has become a well established habit, slight psychic disturbances would not result in enuresis.

SUMMARY

Enuresis was brought about in normal children, from 3 to 4 years of age, merely by transferring them from a large dormitory to small individual cubicles. In some children enuresis was transient, lasting for only forty-eight hours, whereas in others adjustment did not take place during the seven days of observation. When the children were transferred back to the original dormitory enuresis promptly ceased. Psychic enuresis can, therefore, be induced and controlled experimentally, which renders it possible to study various etiologic and therapeutic factors that are commonly associated with this condition.

495 West End Avenue.

5116 Seventeenth Avenue.

ADENOIDS AND IMMUNITY

HENRY B. LEMERE, M.D.
LOS ANGELES

THE ADENOID, A PHYSIOLOGIC STRUCTURE

The inspiration for this paper came from a consideration of the prevalence of sinus trouble in children. One is faced with the problem of an apparent increase in infections of the upper part of the respiratory tract in children which are generally known as sinus trouble. It seems to be impossible to cope with this situation. The hope that removal of tonsils and adenoids would materially reduce such infections has not been fulfilled. Efforts to produce immunity to colds by the injection of vaccines, the feeding of vitamins, and exposure to sunlight and ultraviolet rays are not universally successful; the work here recorded is an effort to discover whether the function of the adenoid is physiologically to tend to produce immunity to, or resolution of, nasal sinus infection in children. "Adenoids" is one of the unfortunate terms of medicine, and even the term "vegetative growths" has been applied to the little structures. These terms seem to preclude the possibility of considering the adenoid organ as a normal physiologic structure. The morphology, gross anatomy and the histology I have considered in a previous paper,[1] and my research at that time convinced me that instead of a pathologic mass, we are dealing with a physiologic structure.

The angle at which an adenoid is viewed with a throat mirror gives the distorted view generally shown in the textbooks, and it appears as a bunch of tissue without form. If care is taken at operation to remove the adenoid in one piece with a large La Force or Kelley[2] instrument, it is found to be a beautiful fanshaped or fleur de lis pattern, four deep

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From the Marion Davies Foundation.

1. Lemere, Henry B.: Adenoids and Pharyngeal Bursa: Their Structure and Morphology, Nebraska M. J. **10**:453 (Dec.) 1925.

2. Kelley, I. D.: Adenoid Removed with Direct Vision Adenotome, Ann. Otol., Rhin. & Laryng. **32**:105 (Dec.) 1923.

furrows dividing five lobes, one central lobe and two lateral lobes. These furrows give an absorbing surface of at least twice the area a smooth pattern gland would give. The minute anatomy is that of normal lymphatic tissue, such as is placed elsewhere in the body to combat invasion. So-called germinal spots of Goodsir are found. These are considered by Latta [3] as areas of cloudy swelling and necrosis rather than germinal spots. They are apparently absorbed, leaving no evidence, and this absorption seems responsible for whatever general reaction this little organ produces against infection. At the lower part of the adenoid, where the furrows converge to a point, there is constantly a cavity lined with mucus membrane and richly supplied with pharyngeal mucus glands. This gives an abundant supply of heavy lubricating mucus, and must aid in promoting adequate closure of the palate in the act of swallowing.

The decision in regard to the adenoid depends largely on the conception of the superficial lymphoid structures of the upper part of the respiratory tract, the tonsils, the adenoid, the lingual tonsil and those masses extending below the tonsil proper. One opinion is that infection resides in the lymphatic tissue, and that it is either permanently there or remains there after secondary implantation and is a source of secondary infection. If this opinion is true, the logical method of procedure would be, as Dr. French says, to remove all suspected lymphoid structures from the throat in as radical a manner as possible, even going far down the pharynx below the tonsil, and on the reappearance of any lymphoid tissue in the nasopharynx, to remove it thoroughly.

The other view is that these structures have a definite physiologic function, but that they may, mechanically, hold infection which, if residual and permanent, may be more harmful than their physiologic function is beneficial.

While these two views do not, at first, appear very divergent, they produce diametric differences of procedure. The first calls for removal of all swollen lymphoid tissue from the throat as pathologic, especially if constitutional conditions indicate a focus of infection in the upper respiratory tract. The other view calls for preservation of lymphoid structures, particularly if this preservation is consistent with free breathing and if the lymphoid structures do not contain permanent or recurrent inclusions of pus; this view thus directs treatment rather to the primary sources of infection in the mouth and nose which are producing the temporary hypertrophy of the tonsil and the adenoid.

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3. Latta: Anat. Rec. **24**:233 (Nov.) 1922.

There is an important difference in the structure of the adenoid and that of the tonsil. The tonsillar crypts and semilunar fold tend to hold and harbor any infection that may gain access to these structures, and by a break in the epithelial lining of the crypts cause systemic symptoms. Clinical observation shows that when once chronic infection occurs in the tonsil it remains until the tonsil is removed. The adenoid presents a different problem. The adenoid rugae or furrows, owing to their anatomic construction, are free to drain and expel any pus carried to them, except rarely when they become ulcerated and adherent and form sacks and pockets. Summarizing, the tonsil is so constructed that it retains infection; the gross construction of the adenoid, however, is such that, generally speaking, it does not retain infection and is healthy tissue, and the pus seen at times on the surface of the specimen removed comes from the posterior drainage of the nose.

COMMON CONCEPTION OF THE ADENOID

The opinion that the adenoid is harmful has run through the years, and until recently no one even questioned the many charges against it. I will try to name them as briefly as possible. It is charged that:

1. The main source of mouth breathing in children is caused by the obstruction due to hypertrophied adenoids.

2. Deafness and discharging ears are due to infection from adenoids and mechanical obstruction from pressure over the mouth of the eustachian tube.

3. They are the cause of sinus disease, which clears up after their removal.

4. Even after their removal a small amount of lymphoid tissue remaining in the nasopharynx may produce all the aforementioned symptoms.

5. Any adenoid found in the nasopharynx should be removed.

During my study of the adenoid the following possibilities came to my mind:

1. The adenoid is a physiologic lymphatic structure with a definite, beautiful form, both grossly and microscopically, admirably designed to expose the greatest possible lymphatic surface as a barrier to the entrance of nasal infection falling into the nasopharynx, and thus gaining access to the general circulation.

2. In children, pus drifts into the adenoid from the nose and sinuses and does not come from the adenoid itself.

3. Occlusions of pus can take place in the adenoid, but they are very rare.

4. The throat may be better if protected by a physiologic adenoid than by the mucous membrane of scar repair resulting after its removal.

5. Mouth breathing is frequently caused by nasal infection.

6. Nasal and nasal sinus infections are greater factors in pathologic conditions in the ear than the mechanical obstruction of adenoids.

In my work in the Marion Davies Children's Clinic I saw an opportunity of following up my cases and testing the truth of this conception of the adenoid. The series on which this paper is based consists of about 150 children operated on during six months' service,[4] most of whom were followed up after operation for weeks and months. In these cases the diseased tonsils were removed and the adenoids left. Exception was made when the child was referred to the nose and throat department with a request for the removal of adenoids and in two cases in which the adenoid was so large as to preclude proper breathing. Examination of the others showed that while the adenoid was often large, there was ample room in the nasopharynx for the free passage of air. When the adenoid was removed a careful inspection of the specimen was made. In no case were there found inclusions of pus or caseous material, such as are seen in tonsils. Once or twice caseous particles were found lying loosely on the adenoid folds, and I think that such particles were expressed when the tonsils were removed and found their way to the adenoid.

The adenoid was examined at the time of operation by finger palpation or direct inspection, care being taken not to traumatize the structure and so cause adhesions and occlusions. I found many medium-sized and large adenoids, but only a few times was there insufficient room between the nose and the adenoid to allow free breathing. These medium-sized and large adenoids were allowed to remain, with the idea that the respiratory obstruction was caused by the insufficient capacity of the nose itself, due to nasal or sinus secretions, swollen turbinates or insufficient development of the nose.

CONSERVATIVE TREATMENT IN TONSIL AND ADENOID OPERATIONS

It was the purpose of this study to try to estimate the good or harm that the adenoid causes.

The patients in this clinic are free from the expense of hospitalization, so that no injustice is done these children if later it is found necessary to subject them to further operation in removing the adenoid. If the parents inquired about the removal of the adenoid it was carefully explained to them that it was left for the purpose of trying to prevent colds and to reduce or to prevent sinus infection.

Four months after following the procedure of removing the infected tonsils and leaving the adenoid, I came across a discussion

4. During the six months that have elapsed between the preparation of the manuscript and the reading of the proof in January, 1932, an additional 150 children have been operated on, making 300 during one year's service.

that occurred on the other side of the Atlantic,[4a] which seems to indicate that the question I am presenting in this paper has arisen in London.

NASAL HYGIENE

To determine the physiologic function of the adenoid by laboratory experimentation seems impossible; to theorize, equally futile. If the children in whom the adenoid is left undamaged when the tonsils are removed respond in a favorable manner, the evidence should be interesting. They are all instructed in the proper hygiene of the nose.

So far as I can learn, animals in a wild state do not suffer from infections of the upper respiratory tract. At least apparently they are never deaf, lose their sense of smell or are chronic mouth breathers. Perhaps this is because their active life leads to much deeper breathing than our civilization demands. Working on this theory, I train the children in whom the adenoid is left to force a draft of air through the air passage in regular morning exercises, the purpose being to expel secretions and to produce aeration of the higher cavities of the nose and of the nasal sinuses. A deep breath is taken and expelled

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4a. Mr. Lowndes Yates said that the development of the nasal sinuses after birth was a subject of great importance in the question of the formation of adenoids. Just before the age of 5 years, the permanent teeth passed into their adult position; the antrum enlarged, the ethmoids began to increase, and shortly afterward they pushed the middle turbinate into the nasal airway. Until then, if a child inhaled a white powder it passed through the nose into the nasopharynx, because the nasal mechanism for the removal of dust and bacteria hardly existed before this age. He thought that adenoids were the infantile mechanism for the removal of dust from the inspired air, and that to take them away too early in cases in which there were no respiratory or aural symptoms and no enlarged glands in the neck, was to deprive the child unnecessarily of this method of protection of the lungs against inhaled infection. After 5 years of age, the adult mechanism for the removal of dust and organisms begins to function, and during the ensuing years of childhood it becomes more functionally complete, until at length it replaces the infantile mechanism.

Mr. T. B. Layton said that it was necessary to go still further back and agree on what was meant by "adenoids," as it seemed clear that Mr. Graham Brown and Mr. Hamblen Thomas had different ideas on the matter from that of Mr. Lowndes Yates. The two former speakers seemed to look on adenoids as pathologic and that they should be removed early in life, whereas Mr. Lowndes Yates looked on them as a physiologic structure, which ought to be conserved as far as possible in early life. Mr. Layton agreed with Mr. Yates. As to the age at which adenoids should be removed, he found himself making it later and later. He did not think Mr. Graham Brown should really be proud of operating on children at the age of 3 years; operation was needed at that age only occasionally. . . . Lymphoid tissue was present to a greater extent in children who were constantly combating a larger number of micro-organisms than they should normally encounter; consequently a child living under bad hygenic conditions needed all its lymphoid tissue, and therefore in the case of children living in overcrowded slums, the operation should not be performed.

forcibly, with both nostrils absolutely free to prevent back pressure through the eustachian tube or even into the sinuses. This exercise is repeated six or eight times in succession once or twice daily. The procedure was outlined by Culbert who called it nasal hygiene.[5] If the material from the nasal and sinus infections is too thick, dry and sticky to be sufficiently removed by these regular air douches, they are preceded by the administration of a mild modified compound solution of sodium biborate (N.F.), so applied that it reaches all the nasal and even part of the sinus mucous membrane, stimulating the mucous membrane and softening the secretions so that the air draft is now able to remove them. Any improvement in drainage of the nasal sinuses from removal of the adenoid can come only from an increased air supply in nasal respiration and from the clearing of the nasal cavities of the retained secretion. I think that both of these results can be attained better by the aforementioned methods of nasal clearance and aeration.

FUNCTION OF THE ADENOID

It seems possible that pus in the nose and sinuses may not be able to produce general reaction and fever, that absorption takes place only when the pus reaches the pharynx, and only then an attempt at immunity occurs. If the adenoid is left, there is a large specialized organ of lymphoid tissue to aid this reaction; if it is removed, the secretion falls on scar tissue covered by repair mucous membrane. If, however, the nose and sinuses do not receive insistent attention, the adenoid may have too much of a load, be drowned in mucopus and become overwhelmed.

I think that too much value may be attached to the subsidence of the phenomena of colds. If this results from the building up of the general resistance and from proper care and hygiene, the gain is real, but if the bacterial infection occurs and the reaction typical of a cold does not take place because of a fibrous and sclerosed nose or lack of general resistance or because the adenoid is removed, the gain is doubtful. It may even be that the absence of the usual symptoms of a cold indicates a loss in the defense against infection of the upper respiratory tract.

FOLLOW-UP TREATMENT

Personal care has been given in each case. Demonstrations have been given to each child how to proceed with treatment. Dates for return visits have been given. When the air draft does not prove efficient, a prescription for the wash and careful instruction as to its use have been given. Inquiry has been made as to the child's food and surroundings. It has been impressed on the parents that this after-treatment is

5. Culbert, W. L.: Tr. Am. Laryng., Rhin. & Otol. Soc., 1924, p. 84.

of more benefit to the child, perhaps, than the tonsillar operation. Even the unintelligent have seemed to understand this, and have been anxious to cooperate.

In private practice, I obtain the same cooperation that I receive in the clinic by making provision for observation of the patient for a year after the tonsillectomy. So far I have had no request for the removal of the adenoids that were left undisturbed, and I have seen no indication to advise it. Colds seem less frequent; no ear troubles supervene, and nasal breathing becomes progressively more free.

Indiscretions of diet, lack of proper protection from changes in temperature, wet feet and other factors render children liable to infections of the upper respiratory tract, so that even when a child is progressing well and following instructions, relapses may occur. However, such relapses are proving relatively infrequent, and this clinical experiment indicates that the adenoid has the function of promoting general resistance to nasal and sinus infections.

EVALUATION OF PROCEDURE

The study of a small group such as this is of little value statistically. Reports on large numbers of school children, such as those of Kaiser [6] and Aycock and Luther,[7] are of great value. Unfortunately, no one in this country (so far as I am aware) has looked on the adenoid as a normal uninfected structure; no one has considered that nasal obstruction in children with adenoids was mainly due to nasal and nasal sinus infections producing thick obstructing secretion and swollen turbinates, and that when relief from these conditions was obtained there was ample room for breathing, even in the presence of a large adenoid. The results of all the statistically reported cases of removal of tonsils and adenoids would be materially modified under a procedure of removing infected tonsils while leaving the healthy adenoids and of giving persistent and prolonged care to the nose. It seems possible that the cases of poliomyelitis developing after operations on the tonsils and adenoids reported by Aycock occurred because of nasal secretions drifting back on a traumatized nasopharynx rather than because the tonsillar fossae were the portal of infection.

As many pediatricians and rhinologists advise the reverse of the procedure herein advised and recommend the removal of the adenoid while leaving the tonsil, it is to be expected that the first reaction to this paper will be antagonistic.

Before condemning this procedure, I should suggest that when the adenoid is removed, it be taken out intact in one piece without mutila-

6. Kaiser, Albert D.: The Relation of Tonsils and Adenoids to Infections in Children, Am. J. Dis. Child. **41**:568 (March) 1931.

7. Aycock, W. Lloyd, and Luther, Eliot H.: New England J. Med. **200**:164 (Jan. 24) 1929.

tion. In order to obtain a good specimen, it is necessary to use the largest size La Force or Kelley instrument with a sharp blade, and to hold it firmly against the back of the upper part of the nasopharynx, since the adenoid is attached to the back of the nasopharynx, and not to the vault, as indicated in many textbooks. With this procedure an intact gland is removed which can be examined grossly and microscopically. While the patient is under anesthesia, before the adenoid is removed, the fingers should be passed into the nasopharynx, not for the purpose of palpation of the adenoid, but rather to determine, by feeling forward to the posterior nares and then backward to the adenoid, the amount of space available for breathing. Even when a large adenoid is present, the space is usually sufficient to allow the finger to move freely forward and backward. In cases in which the adenoid is allowed to remain, persistent and adequate attempts should be made to keep the nose clear, and the air douches should be continued over a period of months or years.

Since I began to write this paper, the excellent critical survey of Selkirk and Mitchell [8] has been published. They justly state that among other disturbing factors the effect of adenotomy alone has not been considered. In the cases reported in the articles they review both tonsils and adenoids were probably removed at the same operation. They observed that the late effects of the combined operation are an increase of sinus infection, headache and growing pains. These would be expected sequelae to adenotomy if the function of the adenoid is to increase immunity to nasal infection.

When I removed the adenoid at the request of the referring physician, the patients were instructed in the nasal clearing exercises, and were followed up. They also showed the value of this after-treatment, which I think is most desirable, whether the adenoid is removed or allowed to remain.

CONCLUSIONS AND SUMMARY

The adenoid is a physiologic and lymphatic structure with a definite form and admirably designed to expose the greatest possible lymphatic surface as a barrier to the entrance of nasal infection through the nasopharyngeal mucosa into the general circulation.

In a series of more than 300 children the adenoids were left at the time the tonsils were removed. Daily expulsive blowing exercises were insisted on as after-treatment. Nasal breathing improved; colds and sinus symptoms and acute and chronic aural conditions were less frequent.

6381 Hollywood Boulevard.

8. Selkirk, Theodore K., and Mitchell, A. Graeme: Evalution of the Results of Tonsillectomy and Adenoidotomy, Am. J. Dis. Child. **42**:9 (July) 1931.

A STUDY OF THE EFFECTS OF ULTRAVIOLET IRRADIATION ON A GROUP OF PRESCHOOL CHILDREN

PRELIMINARY REPORT

HELEN DUDLEY BULL, M.D.

GEORGE H. MAUGHAN, PH.D.

AND

ETHEL B. WARING, PH.D.

ITHACA, N. Y.

This study of a group of healthy preschool children attending the Cornell Nursery School was undertaken in order to determine whether irradiation with ultraviolet rays during the winter months would prove beneficial in lessening illness, particularly colds, in improving hemoglobin, in increasing gains in height and weight or in improving the children's physical condition in other respects.

The children in the Nursery School groups ranged in age from 2 to 5 years. They came from superior homes and lived for the most part on very good hygienic regimens with an opportunity for outdoor play. Their diets were carefully supervised and included ample fruit juices and daily doses of cod liver oil. In spite of these favorable conditions it was found each year that these preschool children lost a great deal of time from illness. The attendance rate in the school has never been above 83 per cent and is sometimes much lower. By far the most frequent cause of these absences was infections due to colds. Colds cause at least 50 per cent of the absences, and some years have accounted for as high as 80 per cent. After most of these colds there was a sharp drop in weight as well as a loss of appetite and general well-being. The winter before this experiment started, hemoglobin estimates and red blood counts were made on all the children at the beginning and end of the winter. Most of the children showed a sharp drop in hemoglobin at the end, the average drop being 14 per cent. The red count showed no appreciable change. It was decided to investigate whether the addition of ultraviolet irradiation for healthy children who were receiving cod liver oil and outdoor play would lessen these unfortunate effects of winter.

The study has been in progress for two winters—1929-1930 and 1930-1931. It is planned to continue it through other winters until a

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large enough number of cases has been accumulated to warrant conclusions, but it has seemed desirable to report the plan of the experiment and the results up to the present time. Although the number of children studied so far has been very small, it has been possible to observe more carefully than usual because of the daily attendance of the physician in the Nursery School and the careful daily records that are kept of each child, both in the school and at home.

METHOD USED IN THIS STUDY

The children in the Nursery School were in two groups. Those who attended the afternoon session were chosen for irradiation, and an equal number of children who attended the morning session were used as controls. The children in the morning control group were slightly

TABLE 1.—*Tabulation of Technic*

	1929-1930	1930-1931
Period of irradiation.....	December 4 to April 18	October 16 to March 26
Number of days per week.....	5 days (except during vacations—Christmas, Farmers' week, Easter)	4 days (except Christmas and Farmers' week)
Actual days of irradiation.....	78 days	80 days
Lamp used	General Electric Sun Lamp	General Electric Sun Lamp
Time of irradiation:		
Average number of irradiations received by each child (allowing for absences)	64½ days	67 days
Range of days irradiated....	No child had less than 56 or more than 73 days	1 child had 80 days, 1 child had only 54 days; the rest were between these

younger than those in the afternoon group. In order to make sure that the age factor did not influence the results, it was thought desirable to add another control group. The first winter this was secured for some items by selecting from past records of the Nursery School an equal number of children of the same ages and comparing the records over a similar period of time at the same month of the year. It seemed obviously unreliable to compare the illness and cold record of one winter against that of another because of the different amount of illness in different winters, but this group served as a control for height and weight increase. The second winter a more satisfactory control group was added from children attending a private play school. Fourteen of these children were examined and followed up through the winter by careful daily records, and seven of the fourteen were found to approximate in age the seven in the irradiated group. These children also received regular outdoor play; five of the seven had cod liver oil daily, and the other two occasionally; the social status of the families was

similar to that of the Nursery School group, but there was not the same close supervision of hygiene and daily regimen.

TECHNIC OF IRRADIATION

The General Electric Sun Lamp, model S1, was used. Lamps were placed so that the children were always within a 6 foot radius of the lights and could continue their ordinary play under the lamps. The children were completely undressed except for a pair of very short, thin, cotton gauze panties. The temperature of the room was 70 F. at the start of treatment. Each year the children began with ten minutes under the lamps. The time was worked up steadily to forty-five minutes daily and kept at this amount. Treatments were given on every school day, and no treatment was given over weekends. The first winter the school week was five days. The second winter it was shortened to four days. Each of the winter holidays, such as Christmas vacation, caused periods of nonirradiation. The first winter the irradiation was not begun until early in December and was continued until April 18. It was decided that probably if it were to be beneficial an earlier start would be more favorable, so the second year the period was begun in mid-October and continued until the end of March. But because of the change from the five to the four day week, the number of days of irradiation proved about the same each year (seventy-eight days the first year and eighty days the second).

Each child was given a complete physical examination before and after the period of study, special note being made of posture, muscle tone, color of the mucous membranes, cavities in the teeth and palpable glands in the neck. Hemoglobin estimates and red blood counts were taken, and the height and weight were recorded. Records of attendance were kept with causes of all absence from school.

RESULTS UP TO THE PRESENT TIME

Number of Children Studied.—Only the children who remained in the school throughout the period were included. The first year (1929-1930) there were eight children who continued throughout the period of irradiation. The second year there were seven. An equal number of children each year was found in the morning Nursery School group, and the second year there was also an equal number in the outside play school group. All these children were classified as healthy at the beginning of the period.

Attendance Record.—The first year the group in which irradiation was given had a better attendance record than the control group of Nursery School children, but the second year exactly the contrary result was found.

Colds.—Colds were recorded by both the number of days of absence due to colds and the average number of colds for each child. The first year the irradiated group had a better record for colds both in absences and in number of colds. (In fairness, however, it should be stated that two children who were not included in this study because they were withdrawn from school before the end of the period happened to have had many colds. The indications are that had they remained the results would have been quite the opposite. The days of absence would have

been increased from ninety-five to one hundred sixty for the irradiated group. The two controls corresponding to these children would have increased the total for this group only from one hundred and nineteen to one hundred and thirty-six. The number of colds would have been the same for each group.)

The second year the irradiated group was compared both with the Nursery School control group and with the group of outside play school children of similar age. This year the first group made a much poorer showing than the Nursery School control group and a slightly poorer showing than the outside play group in days lost by colds. They also made the poorer showing as to the number of colds.

TABLE 2.—*Age Incidence*

	Average Age	Age Range
	1929–1930	
Irradiated group	3 years 11½ months	3 years 7½ months to 4 years 5 months
Morning Nursery School group	2 years 8½ months	2 years 3½ months to 3 years 5 months
	1930–1931	
Irradiated group	3 years 10 months	3 years 4½ months to 4 years 1 month
Morning Nursery School group	3 years 1 month	2 years 10 months to 3 years 4½ months
Outside play school group	3 years 11½ months	3 years to 4 years 5 months

TABLE 3.—*Comparison of the Attendance Records in the Two Groups*

	1929-1930		1930-1931	
	Days of Absence	Percentage of Absence	Days of Absence	Percentage of Absence
Irradiated group	108	17.3	93	16.6
Morning Nursery School group	149	23.9	57	10.0

A monthly record of the number of colds in the irradiated and in the control group was kept to see whether, in the first group, there was more marked falling off in the number of colds in the latter part of the winter (table 5).

Hemoglobin and Red Blood Count.—The hemoglobin readings and the red blood counts are given in table 6. The results as to the hemoglobin the first year were quite surprising as there was a rise instead of the fall that had been obtained previously. The hemoglobin in the irradiated group rose, but not as much as that in the control group. The red blood count was somewhat better for the irradiated group than for the controls. The second year all groups showed a fall in hemoglobin and red blood count, but the irradiated group had a more favorable showing than either of the control groups. The fall in red blood count was also less for the irradiated group. (The Dare hemoglobinometer was used.)

Height and Weight.—Weight: The first year the irradiated group gained less than the control group. The children in the control group were younger, so another group of children of equal age was selected from records of previous years of the Nursery School. The records of their increase in weight over similar months was compared with those of the irradiated group. These children also gained more in weight than those in the group receiving irradiation.

The second year the irradiated group again gained less in weight than the Nursery School group, but the first group did gain much more than the outside play group. (This may indicate the superiority of the regular Nursery School regimen rather than other differences.)

TABLE 4.—*Cold Incidence*

	School Days Lost by Colds	Percentage of Days Lost by Colds	Average Number of Colds per Child
	1929–1930		
Irradiated group	95	15.2	2.12
Morning Nursery School group	119	19.0	2.62
	1930–1931		
Irradiated group	75	13.3	3.14
Morning Nursery School group	36	6.5	1.14
Outside play school group	73	13.0	2.55

TABLE 5.—*Monthly Record of the Number of Colds*

	Dec.	Jan.	Feb.	March	April	May
	1929–30					
Irradiated group	4	10	6	8	0	0
Morning Nursery School group	4	6	4	12	2	0
	1930–1931					
Irradiated group	2	5	4	4	3	4
Morning Nursery School group	2	2	0	0	11	1
Outside play school group	2	0	4	7	6	0

Height: The morning Nursery School group each year gained more in height than the irradiated group, but as the children were younger this might have been expected. The first year the gain in height was the same for the irradiated group as for the children of the same age described as controls.

The second year the gain in height for the irradiated group was less than that for the outside control group.

Physical Examinations.—Careful physical examinations were made on all children both years before and after the period of irradiation, but the second year comparison was made on several selected points. The findings were inconclusive, particularly because of the small number. For this reason the records are not given in detail, but are briefly summarized.

Muscle Tone: There was no change noted in either of the two control groups, and in the irradiated group there was no marked change, but there were two children who were noted as improved.

Posture: There seemed to be more gain in posture in the group receiving irradiation than in the control groups.

Color (Pallor of the Mucous Membrane): It was difficult to say that one group had any advantage over the other.

Teeth: Most of the children had good teeth all of the time (as is usual with the children in this Nursery School). No child in the group receiving irradiation developed cavities during the period, whereas one

TABLE 6.—*Hemoglobin and Red Blood Counts*

	Average Hemoglobin, per Cent					
	1929–1930			1930–1931		
	Before Irradiation Period	After Irradiation Period	Comparison	Before Irradiation Period	After Irradiation Period	Comparison
Irradiated group	72.2	84.1	+ 8.9	80.0	79.6	— 0.4
Morning Nursery School group	73.0	86.4	+13.4	77.5	74.5	— 0.3
Outside play school group	....	....	.....	78.5	76.5	— 0.2
	Red Blood Counts					
Irradiated group	4,427,000	4,887,000	+460,000	4,876,000	4,335,000	—541,000
Morning Nursery School group	4,307,000	4,038,000	—269,000	4,881,000	3,919,000	—962,000
Outside play school group	.....	.....	.....	4,946,000	4,182,000	—764,000

TABLE 7.—*Average Gains in Weight and Height During the Period of Irradiation*

	1929-1930		1930-1931	
	Weight, Ounces	Height, Inches	Weight, Ounces	Height, Inches
Irradiated group	22.5	1.125	40	0.842
Morning Nursery School group	27.1	1.490	43	0.885
Outside play school group	....	.....	26	0.974
Control group of similar age from past records	26.5	1.125		

child in the morning Nursery School and two children in the outside group did develop cavities during the period.

Palpable Glands in the Neck: Two children in the irradiated group had slightly enlarged glands in the neck before the period of irradiation, and these had disappeared at the end. In the outside play school group in which the children did not receive irradiation the same results were obtained; two were found at the beginning with palpable glands in the neck, and these had disappeared at the end.

Home records of the children were kept as to the appetite and general condition, such as fatigue, etc. Also the subjective judgment of the mother was recorded as to the effect of the treatment, but nothing conclusive could be drawn from these records to suggest any change that might be due to irradiation.

PLANS FOR THE FOLLOWING WINTER

It is planned to continue the experiment in general as carried out previously, starting early in October and continuing until the first of April. It is planned to add another small group of children who will take daily irradiation, including weekends and vacations, to determine, if possible, whether the interruptions in the treatment may in any way influence the results.

SUMMARY

Irradiation by mercury vapor lamps in moderate doses on each school day during the winter months was given to a group of healthy children who also received cod liver oil and an opportunity for outdoor play. This was undertaken because nursery school children have been found during previous years to suffer markedly from colds, low hemoglobin and other ill effects of the winter months. For the two winters in which observations have been made it has not been possible as yet to find either any improvement in the illness rate, in the number or severity of colds, and in the hemoglobin and red blood count or marked changes in physical status which could be attributed to the irradiation.

ANTIRACHITIC VALUE OF MILK FROM COWS FED IRRADIATED YEAST

EDWIN T. WYMAN, M.D.
AND
ALLAN M. BUTLER, M.D.
BOSTON

The experiments of Thomas and MacLeod [1] have shown that the incorporation of from 30,000 to 60,000 rat units per day of vitamin D as irradiated yeast in the diet of a dairy cow results in the production of a milk high in antirachitic properties. This effect of feeding irradiated yeast has also been reported by Steenbock and co-workers [2] and by Wachdel.[3] The results of Thomas and MacLeod not only show the effective antirachitic quality of such milk as measured by bioassays on rats, but also indicate that on the basis of rat units fed, irradiated yeast is approximately three times as effective in producing antirachitic properties in milk as viosterol (irradiated ergosterol). The studies of Hess, Lewis, MacLeod and Thomas [4] have demonstrated that the substitution of milk produced by cows fed 60,000 vitamin D rat units per day as irradiated yeast for the ordinary cow's milk in the formulas of infants is an effective prophylactic agent against rickets and is curative in cases of moderate rickets. Their paper indicates the particular potency in terms of antirachitic rat units of irradiated yeast in the production of antirachitic milk, and suggests that the activity of "yeast milk" resembles that of cod liver oil rather than that of viosterol. In this connection it is interesting to recall that Steenbock and his co-workers reported evidence that vitamin D in yeast occurs in at least two different forms.

Because of the possibility of difference in the specific factors in "yeast milk" and viosterol, and because there are certain advantages in the inclusion of the antirachitic factor in the food of infants rather than adding it as a separate therapeutic agent, we have studied the

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From the Infants' and Children's Hospitals and the Department of Pediatrics, Harvard Medical School.

This work was undertaken at the suggestion of Dr. Richard S. Eustis, and the special yeast milk was provided through his cooperation.

1. Thomas, B. H., and MacLeod, F. L.: Science **73**:618, 1931.
2. Steenbock, H.; Hart, E. B., and Hanning, F.: J. Biol. Chem. **88**:197, 1930.
3. Wachdel, M.: München. med. Wchnschr. **76**:1513, 1929.
4. Hess, A. F.; Lewis, J. M.; MacLeod, F. L., and Thomas, B. H.: Antirachitic Potency of the Milk of Cows Fed Irradiated Yeast or Ergosterol, J. A. M. A. **97**:380 (Aug. 8) 1931.

effectiveness of such "yeast milk" in the healing of active rickets in children. Since undertaking the work, "yeast milk" has been placed on the market by the Walker Gordon Laboratory Company. The work reported herein has, therefore, acquired a certain additional value by contributing to the data available for the appraisal of this new therapeutic agent by the pediatrician.

OUTLINE OF EXPERIMENTS

Two infants and two children admitted to the Infants' and Children's Hospitals because of advanced active rickets were selected for this study. A brief history and the significant physical findings in each case will be presented with the results of the experiments. On admission the patients were placed in a ward and given a simple diet adequate for their caloric requirements. Each subject was then observed for a period of from ten to twenty-three days to make sure that healing was not taking place. In order to determine this, roentgenograms of the long bones were taken, and the calcium and inorganic phosphorus contents of the serums were determined at regular intervals. In the taking of blood samples and separation of the serum, care was taken to avoid hemolysis. The serums were separated immediately and the inorganic phosphorus determined at once. Calcium was determined by the method of Fiske and Logan,[5] 2 cc. of serum being used for each determination, and inorganic phosphorus was determined by the method of Fiske and Subbarow.[6] Having satisfied ourselves in this control period that healing was not occurring, the milk in the diet of each child was replaced by the special "yeast milk."

This milk was produced under the supervision of Dr. B. H. Thomas at the Charles River farm of the Walker Gordon Laboratory Company. Eighteen recently freshened cows from their "certified" dairy herd were used. The group was comprised of Holstein-Friesian, Jersey, Guernsey and Ayrshire females, milking between 25 and 35 pounds (11 to 15 Kg.) of 4 per cent milk daily on a two-time milking schedule. Their basal ration consisted of 30 pounds (13.6 Kg.) of corn silage, 12 pounds (5.4 Kg.) of chopped alfalfa and clover hay, 4 pounds (1.8 Kg.) of soaked beet pulp, and 12 pounds of a 17 per cent protein grain mixture. Nine of the cows received, in addition, 60,000 rat units as irradiated yeast daily. The milk produced by these nine cows was used as the special "yeast milk." The remaining nine cows received the basal ration and were held as replacements in the event that any of the experimental animals had to be withdrawn during the course of the experiment. The cows were stanchioned in a barn except when exercised in a pad-

5. Fiske, C. H., and Logan, M. A.: J. Biol. Chem. **93**:211, 1931.
6. Fiske, C. H., and Subbarow, Y.: J. Biol. Chem. **66**:375, 1925.

dock free from vegetation. The appearance, appetites and quantity of milk produced was normal for all the cows throughout the experiment.

In the experiments on the first three patients this milk was pasteurized before being fed. In addition to being pasteurized, the milk, before being fed to the fourth patient, was boiled for five minutes. In every other respect the routine was continued as nearly as possible as in the control period. The subjects were confined in bed in the wards throughout the entire time. Roentgenograms were taken and serum calcium and phosphorus [7] determinations made in order to follow the progress of the therapy. During the period of study the children made satisfactory gains in weight. One of the subjects (case 1) was placed on a metabolism bed during the control and the special milk periods, and studies were made of the phosphorus and calcium balances. The results of this study will be reported in a separate paper.

RESULTS

Case 1.—D. E., an American boy, 16½ months of age, was admitted to the Infants' Hospital on March 31, 1931, with the diagnosis of active rickets. He was breast fed for the first six months and was given milk, sugar and water supplements from the third to the sixth month. Orange juice and cod liver oil had been given in irregular amounts since the third month. The cod liver oil had never exceeded 1 fluid drachm (4 cc.) per day and had not been given recently. Physical examination showed an underdeveloped but fairly well nourished, anemic Negro infant. Prominent bosses, a rachitic rosary and Harrison's groove, enlarged epiphyseal ends of the long bones and bilateral bowing of the tibia and femur were present. He weighed 18 pounds (8,200 Gm.). On admission he was placed on the following diet: whole milk, 32 ounces (946 cc.); cereal (farina), 13.3 Gm.; banana, 100 Gm., and orange juice, 1 ounce (30 cc.). The calcium-phosphorus product at entry was 34.3. Roentgenograms showed a slight deposition of opaque salts in the osteoid tissues at the end of the diaphyses. During the control period the calcium-phosphorus product dropped (table 1) so that on April 23 it was 23.3 In the three week control period the inorganic serum phosphorus fell from 3.3 mg. to 2.4 mg. per hundred cubic centimeters. This is evidence against the presence of any significant amount of latent rachitic healing following interrupted therapy. For, as shown by Gerstenberger, Hartman, Russell and Wilder,[8] had such healing been present, the serum phosphorus should have risen. The roentgenograms taken during the control period also showed no detectable change. Therefore, we felt that latent healing following interrupted antirachitic therapy could be ruled out, and we considered this case suitable for study. On April 23, 1931, the pasteurized special milk was substituted for the ordinary milk of the diet. On May 5, the amount of milk was increased from 32 to 40 ounces (946 to 1183 cc.) Except for these changes, the routine and diet were maintained constant during the ten weeks of hospitalization. On June 9, the boy weighed 19.6 pounds (8,855 Gm.). Table 1 gives in summary form the

7. Phosphorus is used throughout the rest of the paper instead of the fuller term in organic serum phosphorus.

8. Gerstenberger, H. J.; Hartman, J. I.; Russell, G. R., and Wilder, T. S.: The Etiology of Infantile Spasmophilia, J. A. M. A. **94**:523 (Feb. 22) 1930.

results obtained from the chemical determinations and roentgenograms. Figure 1 gives reproductions of four of the roentgenograms from this case.

Case 2.—D. F., an American boy, 8 months of age, was admitted to the Infants' Hospital on March 17, 1931, with a condition diagnosed as active rickets. He was breast fed for two months. Since then he had been on a well balanced formula of cow's milk. Cereal was added at the fourth month. Since the third month he had had the juice of one orange every day. He had never received cod liver oil, viosterol or ultraviolet treatments. Physical examination showed a well developed and well nourished infant breathing rapidly with a soft expiratory and

Table 1.—*Summary of Case 1, D. E., Aged Sixteen Months*

Date, 1931	Weight, Pounds	Calories per Pound	Serum Calcium, Mg. per 100 Cc.	Serum Phosphorus, Mg. per 100 Cc.	Calcium–Phosphorus Product	Roentgenograms
March 31	18.0	45.0	10.4	3.3	34.3	Advanced active rickets; slight deposition of tricalcium phosphate in osteoid tissue
April 13	18.0	45.0	10.7	2.5	26.8	No further change
April 23*	18.3	43.8	9.7	2.4	23.3	No further change
May 5	18.7	51.6	11.8	5.5	64.9	Healing rickets
May 18	19.5	49.5	11.4	5.9	67.3	Further healing
June 9	19.6	49.1	11.5	5.7	65.6	Further healing

* Special milk started.

Table 2.—*Summary of Case 2, D. F., Aged 8 Months*

Date, 1931	Weight, Pounds	Calories per Pound	Serum Calcium, Mg. per 100 Cc.	Serum Phosphorus, Mg. per 100 Cc.	Calcium–Phosphorus Product	Roentgenograms
March 18	....	....	....	...	....	Advanced active rickets; slight deposition of tricalcium phosphate in osteoid tissue
March 25	16.5	43.5	7.8	3.5	27.3	No further change
March 26*	....	....	....	...	....	
March 30	16.8	42.6	8.2	3.7	30.3	No change
April 13	16.9	52.1	10.0	4.7	47.0	Healing rickets
April 30	17.5	50.6	10.3	4.4	45.3	Further healing
May 11	17.9	55.5	11.2	6.2	69.4	Further healing
June 8*†	18.6	....	....	...	....	Almost healed

* Special milk started.
† After three weeks at home where special yeast milk was continued.

inspiratory sound. The intercostal spaces and ribs were drawn in on inspiration. Marked craniotabes, Harrison's groove, rachitic rosary and enlarged epiphyseal ends of the long bones were present. The infant weighed 16.7 pounds (7,650 Gm.). On admission to the hospital he had an acute infection of the upper part of the respiratory tract, and slight bronchopneumonia with a temperature of 102 F. Two days later the chest signs disappeared, and the temperature fell to normal and remained so throughout the course of the experimental period. The patient was placed on a diet consisting of 32 ounces of whole milk, 15 Gm. of cereal, 100 Gm. of banana and 1 ounce of orange juice. Because of the evidence from the roentgenograms and the values for serum calcium and phosphorus and because of the definite absence of antirachitic therapy in the history, it was felt that any healing taking place in this patient was insignificant, and that he was suitable for

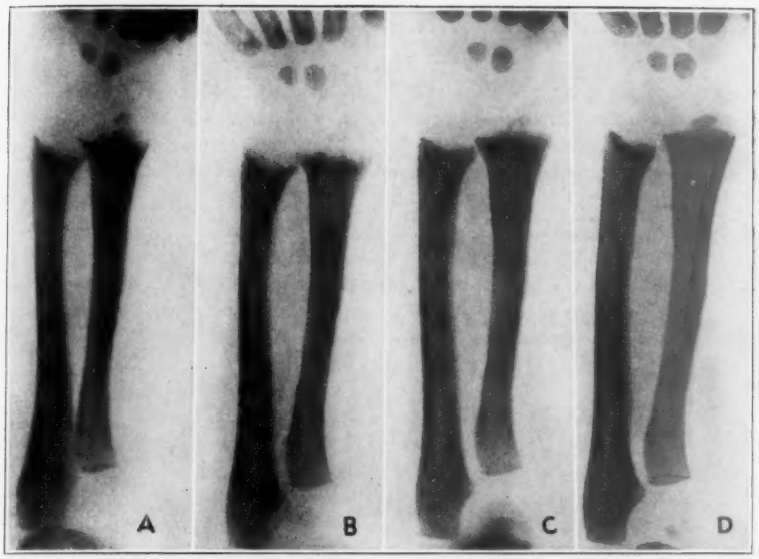

Fig. 1 (case 1).—Roentgenograms of the radius and ulna of D. E., aged 16 months. *A*, taken March 31, showing advanced active rickets with slight deposition of tricalcium phosphate in osteoid tissue; *B*, taken April 23, showing no further change during control period; *C*, taken May 9, after sixteen days on the special milk, showing healing rickets, and *D*, taken June 9, showing further healing.

Fig. 2 (case 2).—Roentgenograms of radius and ulna of D. F., aged 8 months. *A*, taken March 18, showing advanced active rickets, with slight deposition of tricalcium phosphate in osteoid tissue; *B*, taken March 25, showing no further change during control period; *C*, taken April 21, after twenty-six days on the special milk, showing healing rickets, and *D*, taken June 8, showing almost completely healed rickets.

our study as having an advanced case of active rickets. The pasteurized special milk was substituted for the ordinary milk on March 26. On May 11, he weighed 17.9 pounds (8,150 Gm.). Table 2 presents the summary of results obtained in this case. Figure 2 shows four roentgenograms taken in case 2.

CASE 3.—P. O., a colored girl, 4 years and 11 months of age, was admitted to the Children's Hospital on March 31, 1931, with a condition diagnosed as active rickets with marked bony deformities. She was delivered prematurely at 8 months because of her mother's hypertension and kidney condition. Her birth weight was 4.5 pounds (2,050 Gm.). For the first two months she did well on breast milk. For the next eleven months she received various formulas and did poorly. During this period she received orange juice, and irregularly 4 cc. (1 fluid drachm) of cod liver oil was given three times a day. After eighteen months the orange juice and cod liver oil were discontinued. She sat up at 1 year of age and walked at the age of 3. The first teeth appeared when she was 1 year old. At the age of 2.5 years her mother noticed that her wrists were extraordinarily large, and noted that they continued to increase. When the child started to walk, soreness and bending of the legs developed, and these conditions continued to become worse.

TABLE 3.—*Summary of Case 3, P. O., Aged 5 Years*

Date, 1931	Weight, Pounds	Serum Calcium, Mg. per 100 Cc.	Serum Phosphorus, Mg. per 100 Cc.	Calcium-Phosphorus Product	Roentgenograms
March 31	....	....	...	....	Advanced chronic rickets; slight deposition of tricalcium phosphate in osteoid tissue
April 7	32.0	10.4	3.2	33.3	
April 15*	....	....	...	....	No change
April 16	....	10.7	3.5	37.5	
April 29	34.0	11.3	4.2	47.5	Healing rickets
May 13	....	11.4	6.0	68.4	Further healing
May 23	37.0	....	...	....	Almost healed

* Special milk started.

For a year before the mother consulted us the child's diet had consisted of abundant vegetables, a small amount of meat, a moderate amount of milk and a moderate amount of sweets. She had received no cod liver oil, viosterol or ultraviolet therapy since 18 months of age.

Physical examination showed a well nourished colored child, small for her age. The frontal bosses were prominent. Flaring of the thorax, rachitic rosary, Harrison's groove and enlargement of the epiphyseal ends of the long bones were present. There was marked lateral and anterior bowing of the tibia and marked deformity at the ankles. Her weight was 32 pounds (14,500 Gm.). On admission she was placed on a ward diet without antirachitic substances. On April 14 a mistake was made in writing the orders for this patient and as a result she received on that day, 30 minims (1.9 cc.) of viosterol. Roentgenograms on April 15 showed no change from those taken March 31. On April 15, pasteurized special milk was substituted for the ordinary milk in her diet. This milk was given in amounts of from 32 to 40 ounces a day. On April 16, the serum calcium was 10.7 mg. per hundred cubic centimeters and inorganic phosphorus 3.5 mg. making the calcium-phosphorus product 37.5, as compared with a calcium-phosphorus product of 33.3 on April 7. As the roentgenograms on the previous day gave evidence against any healing and no cause for healing could be ascertained other than the 30 minims of viosterol and the special yeast milk given one

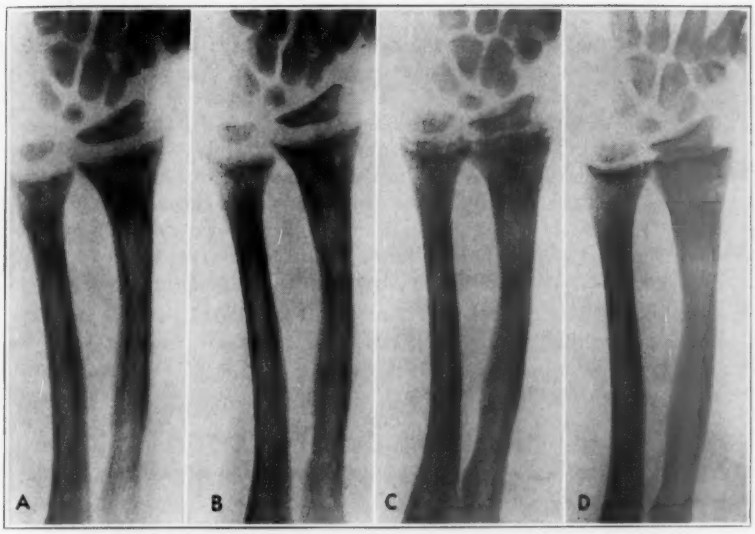

Fig. 3 (case 3).—Roentgenograms of the radius and ulna of P. O., aged 5 years. *A*, taken March 31, showing advanced chronic rickets with slight deposition of tricalcium phosphate in osteoid tissue; *B*, taken April 15, showing no change during control period; *C*, taken April 29, after thirteen days on the special milk, showing healing rickets, and *D*, taken May 23, showing almost completely healed rickets.

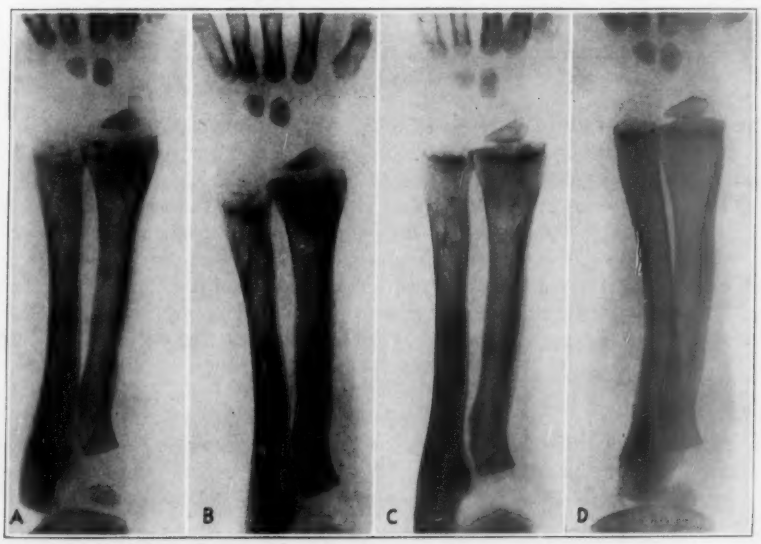

Fig. 4 (case 4).—Roentgenograms of the radius and ulna of L. J., aged 3 years. *A*, taken May 20, showing advanced chronic rickets with moderate deposition of tricalcium phosphate in osteoid tissue; *B*, taken May 25, showing no change during control period; *C*, taken June 22, after twenty-seven days on the boiled special milk, showing healing rickets, and *D*, taken July 28, showing further healing.

day, we assumed that this rise in the calcium phosphorus product was the result of the past two days therapy, and that healing had not occurred between March 31 and April 14. It was further felt that the small amount of viosterol given would not interfere with the validity of the experiment. The rapidity with which almost complete healing occurred in contrast to what might have been expected from the amount of viosterol given or the presence of a latent healing is such as to leave little doubt that the healing was the result of the ingestion of the special yeast milk. Had healing been due to the other agents we would have expected the amount of serum calcium to have fallen.[8] Table 3 presents the summary of the findings in this case. Figure 3 shows four of the roentgenograms taken in case 3.

CASE 4.—L. J., a colored girl, 3 years and 2 months of age, was admitted to the Children's Hospital on May 16, 1931, with a condition diagnosed as active rickets. She had been a full term baby who was breast fed for eighteen months. Orange juice was first given at 6 months of age. She sat up at 10 months, walked at 30 and talked at 26 months. The first teeth appeared at 8 months. Even since the child was an infant the mother had noticed the enlargement of the wrists, the square head and the small chest. As soon as the child walked her legs became

TABLE 4.—*Summary of Case 4, L. J., Aged 3 Years*

Date, 1931	Weight, Pounds	Serum Calcium, Mg. per 100 Cc.	Serum Phosphorus, Mg. per 100 Cc.	Calcium-Phosphorus Product	Roentgenograms
May 20	19.4	10.9	3.1	33.8	Advanced chronic rickets; moderate deposition of tricalcium phosphate in osteoid tissue
May 25*	19.6	10.9	2.7	29.4	No change
June 9	20.7	10.9	3.5	38.2	Healing rickets
June 22	21.0	11.1	4.5	49.3	Further change
June 30	22.0	11.3	5.2	58.8	Further change
July 6	22.4	11.0	5.0	55.0	Further change
July 16	22.7	11.4	4.4	50.2	Further change

* Special milk started.

bowed. She was slow in learning to walk and had always been weak. For six months prior to admission she had been on a mixed diet containing fresh fruit. Until two and one half months prior to admission she had never received cod liver oil or viosterol. For the preceding two and one half months she supposedly had received 8 cc. of cod liver oil a day, but this had been taken very irregularly. During this period she had been outdoors very little. Physical examination showed prominent frontal bosses, marked deformity of the chest with flaring ribs, Harrison's groove and rachitic rosary, marked enlargement of the epiphyseal ends of the long bones and outward bowing of the tibia. She weighed 19.4 pounds (8,800 Gm.). During the past two months some healing undoubtedly had occurred. The inorganic serum phosphorus had risen from 2 mg. per hundred cubic centimeters to 3.1 mg., and roentgenograms taken on May 10 and 22 showed moderate deposition of calcium phosphate in the osteoid tissue in the lower ends of the radius and ulna.

On admission to the hospital, on May 16, 1931, a diet similar to that used in case 3 was given. No substances containing antirachitic properties were given. On May 25 the inorganic serum calcium remaining the same, namely 10.9 mg., the inorganic serum phosphorus had fallen to 2.7 mg. Roentgenograms showed the same condition as on admission. Due to the fact that healing may occur for long periods following the cessation of antirachitic therapy,[8] we are aware that this

case was not properly controlled. However, we wished to test the efficacy of the boiled special milk, and this was the only available patient. On May 25 the boiled special yeast milk was substituted for the ordinary milk in the diet, about 32 ounces per day being taken. The milk was boiled for five minutes in addition to being pasteurized. On July 16, the patient weighed 22.7 pounds (10,350 Gm.). Table 4 summarizes the results obtained during the study of this case. Figure 4 shows four roentgenograms.

Comment.—The fall in serum phosphorus in the control period of case 4, the rise in serum phosphorus with the substitution of the special milk and the maintenance of a high serum calcium throughout the following two months in the presence of active healing give evidence that the boiled special milk had definite antirachitic properties. But being unable to appraise the proportion of the total healing due to the action of the interrupted cod liver oil therapy, the results, which show a slight delay in the augmentation of the calcium-phosphorus product and a longer

TABLE 5.—*Calcium and Phosphorus Before and After Special Milk was Added to the Diet*

Case	Name	Age	Length of Time on the Milk, Days	Serum Calcium, Mg. per 100 Cc.		Serum Phosphorus, Mg. per 100 Cc.		Calcium-Phosphorus Product	
				Before	After*	Before	After	Before	After
1	D. E.	16 mo.	25	9.7	11.4	2.4	5.9	23.3	67.3
2	D. F.	8 mo.	46	7.8	11.2	3.5	6.2	27.3	69.4
3	P. O.	4 yr., 11 mo.	28	10.4	11.4	3.2	6.0	33.3	68.4
4	L. J.	3 yr., 2 mo.	36	10.9	11.3	2.7	5.2	29.4	58.8

* The selection of the data to be placed under the caption "after" has in each case been determined by taking the day of the highest calcium-phosphorus product.

period for complete healing compared to case 3 do not furnish us with data on which to base an opinion concerning the possible diminution of the milk's antirachitic potency by boiling.

Table 5 summarizes the results of the calcium and phosphorus determinations throughout the four experiments.

COMMENT

Deposition of bone as shown by roentgenograms could be seen approximately two weeks after the administration of the pasteurized special milk and continued at a satisfactory rate throughout the period of observation. The administration of the pasteurized special milk for two weeks resulted in a rise in the serum phosphorus and a marked increase in the calcium-phosphorus product.

In cases 1, 2 and 3, after the patient had been on the pasteurized yeast milk for approximately two weeks, the calcium-phosphorus product had risen to 47 mg. or above. In case 4, after the patient had been on the boiled yeast milk regimen for two weeks, the product had risen to 38.2, but roentgenograms showed definite healing. At the

end of twenty-eight days on the boiled yeast milk diet, the calcium-phosphorus product had risen to 49.3. Though healing continued to complete recovery, it did not take place as rapidly as in case 3, in which almost complete healing occurred in six weeks. The uncertainty in interpretation of the results of this last experiment has been pointed out previously.

Howland and Kramer [9] have stated that "the determining factor in calcification of the bones is the presence of calcium and phosphorus in such amounts that the product of their concentration in milligrams per hundred cubic centimeters of serum equals a certain minimum figure which lies roughly between 30 and 40." From the data reported here it would seem that a calcium-phosphorus product of less than 30 had to be reached before the deposition of a calcium phosphate, opaque to the x-rays, in osteoid tissue ceased. When the calcium-phosphorus product was roughly from 30 to 34, calcium phosphate was deposited, but the deposition was insufficient to provide adequately for the growing osteoid tissue in these growing children. In case 4 sufficient deposition of calcium phosphate occurred with a calcium-phosphorus product of 38 to permit the appearance of healing of advanced rickets as determined by roentgenograms. These figures would lead one to believe that the presence of a calcium-phosphorus product of approximately 30 permitted calcium phosphate deposit in bone. The value of the calcium-phosphorus product which in a given case will permit complete calcification of osteoid tissue probably depends on the rate of growth of the individual.

SUMMARY

1. The special pasteurized yeast milk was an effective source of antirachitic substance as determined by its ability to cause healing in advanced active rickets in infants and advanced chronic rickets in children. After five minutes' boiling the milk still possessed antirachitic properties.

2. The administration of antirachitic vitamin in so palatable a form and in a food so essential and generally used as milk would seem to have certain advantages. The substitution of this milk for the ordinary milk in the formulas of infants would introduce an effective prophylactic and curative agent against rickets requiring a minimum of cooperation on the part of the mother.

3. The data present evidence concerning the value of the calcium-phosphorus product at which calcium phosphate deposition may occur in osteoid tissue.

Dr. E. C. Vogt cooperated in taking the many roentgenograms and gave advice in their interpretation.

9. Howland, J., and Kramer, B.: Tr. Am. Pediat. Soc. **34**:204, 1922.

STUDY OF THE WATER AND MINERAL BALANCES IN EPILEPTIC CHILDREN

I. EFFECTS OF DIURESIS, CATHARSIS, PHENOBARBITAL THERAPY AND WATER STORAGE

IRVINE McQUARRIE, M.D.
MINNEAPOLIS
AND
R. C. MANCHESTER, M.S.
AND
CLARA HUSTED, M.S.
ROCHESTER, N. Y.

That there is some significant relationship between the water balance of the body and the occurrence of convulsive seizures in epilepsy has been demonstrated by the clinical observations of Fay [1] and others and by our experimental studies [2] and those of Gamble and Hamilton.[3] There is no agreement of opinion, however, regarding the underlying nature of this relationship, although several tentative explanations have been offered.

Gamble and Hamilton, who were primarily concerned with the problem of the total acid-base metabolism, observed that urinary water, as well as total base and acid, was considerably increased during the convulsive phase as contrasted with the nonconvulsive phase of the disease. The increment in both base and water excretion was interpreted as being incidental to the elimination of the extra acid released from

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From the Departments of Pediatrics, University of Rochester, Rochester, N. Y., and University of Minnesota, Minneapolis.

1. Fay, Temple: Some Factors in the "Mechanical Theory of Epilepsy" with Especial Reference to the Influence of Fluid, and Its Control, in the Treatment of Certain Cases, Am. J. Psychiat. **8**:783, 1929.

2. McQuarrie, Irvine: Epilepsy in Children: The Relationship of the Water Balance to the Occurrence of Seizures, Am. J. Dis. Child. **38**:451 (Sept.) 1929. McQuarrie, Irvine; Manchester, R. C., and Husted, Clara: The Effect of Induced Changes in the State of Hydration upon the Occurrence of Convulsions in Epileptic Children, in Epilepsy and the Convulsive State, Proc. A. Research Nerv. & Ment. Dis., Baltimore, Williams & Wilkins Company, 1932, vol. 7, p. 623.

3. Gamble, J. L., and Hamilton, B.: The Acid-Base Composition of the Urine from an Epileptic, Bull. Johns Hopkins Hosp. **41**:389, 1927.

the body tissues during the convulsions. Since the extra total acid excreted was composed chiefly of chloride ion and the extra total base of sodium (as estimated by difference), the logical conclusion was drawn that the water lost had its origin in the extracellular body fluid.

Fay attributed the favorable therapeutic results from water restriction in epilepsy, which he first reported, to reduction of hydraulic pressure within the skull. It is his belief, based on certain anatomic observations of Weed,[4] Mixter[5] and Winkelman,[6] that the underlying or predisposing cause of epilepsy is some pathologic condition of the arachnoid villi or the pacchionian bodies, which tends to interfere with their supposed special function of absorbing fluid from the subarachnoid space. He assumes that there is an imbalance in active epilepsy between the production and absorption of cerebrospinal fluid with damming back of the latter under increased pressure within the subarachnoid space. With this condition as a predisposing cause, any one of a great variety of factors, such as circulatory changes, anoxemia or alkalosis, acting as a precipitating cause, may set off the convulsion. According to this view, the total water balance of the body is of importance so far as it leads to an increase or a decrease in the volume of fluid in the subarachnoid space.

In contrast with this purely mechanical point of view, our own tentative explanation of the fact that a deficit in water balance tends to prevent seizures while storage of water favors their occurrence was that the physiologic mechanism for governing the water exchanges of the brain cells tend to function erratically in the epileptic subject, especially when placed under strain. It was considered that excessive imbibition of water by the cells would probably account for widespread increased irritability and the resulting convulsion. It was tentatively assumed that the beneficial effect of therapeutic measures which maintain the water stores at fairly low levels was due to their preventing overhydration of the brain cells. This interpretation was admittedly tentative in character, because the experimental data for testing its validity were not available. The present investigation on the mineral as well as the water metabolism was undertaken with the hope of further elucidating the nature of these relationships.

PLAN OF RESEARCH AND METHODS USED

In this study, consisting of an uninterrupted succession of experiments on a single patient over a period of more than five weeks, the water intake was main-

4. Weed, L. H.: The Cerebrospinal Fluid, Physiol. Rev. **2**:171, 1922.

5. Mixter, W. J.: Three Cases of Focal Epilepsy, Arch. Neurol. & Psychiat. **9**:402 (March) 1923.

6. Winkelman, N. W.: Pathological Studies of the Arachnoid Villi and Pacchionian Bodies in Various Types of the Convulsive State, in Epilepsy and the Convulsive State, Proc. A. Research Nerv. & Ment. Dis., Baltimore, Williams & Wilkins Company, 1932, vol. 7, p. 502.

tained at a level calculated to be sufficient to meet her physiologic requirements under ordinary conditions. That the amount allowed was adequate in this respect is shown by the results of the initial three day control period. One of the objects in view was to determine whether or not the absolute levels of water and mineral exchange might be of importance aside from the effect of net balance. For this purpose the routine level of intake was kept relatively high, while the effects of diuresis, catharsis, forced water drinking, phenobarbital (phenylethylbarbituric acid) therapy and pituitary antidiuresis were successively determined.

The total water balance was measured essentially according to the procedure outlined by Johnston and Newburg,[7] to whom we are indebted for many valuable suggestions given in advance of the publication of their paper. During the first week of the study the environmental temperature daily rose above the critical point for visible sweating, although it remained definitely below this point thereafter. The total loss of water due to sweating was calculated from weight changes. The insensible water for these few days was assumed to be equal to that found for the same patient on other days under ideal conditions. The room temperature and relative humidity, which were taken hourly, ranged from 21 to 26 C. and from 40 to 74 per cent, respectively, throughout the last four weeks of the study.

The diet, which was kept uniform throughout the entire period, was sufficient for maintenance of body weight and nitrogen balance under ordinary conditions. The metabolic mixture, as estimated by the method of Newburg and Johnston,[8] had a ketogenic to antiketogenic ratio slightly less than unity. For the sake of uniformity and accuracy of analysis, simple foods were used. Dried, whole-milk powder ("klim"), egg yolk, fresh 40 per cent cream, cane sugar, clear lemon juice and distilled water constituted the diet. To avoid repetition of analysis, the milk powder was obtained in bulk sufficient to meet the demands for the entire study. In addition to one complete analysis of a composite sample of the cream used, analyses of the fresh cream were made daily for fat and nitrogen content. All foods were analyzed for their water and mineral constituents as well as for protein and fat. The carbohydrate content was estimated from standard food tables. No minerals were added to the diet.

The patient selected for this study was a girl, aged 15 years, with unusually severe epilepsy, who rarely had a single day without grand mal seizures, when not under intensive antiepileptic treatment. Although she had had seizures with increasing frequency and severity for six years with a moderate degree of mental retardation, she was essentially normal in other respects. She was reasonably cooperative throughout the entire study, but appeared especially bright and cheerful during periods of freedom from convulsions.

She was kept in a small metabolism ward with another more intelligent epileptic girl under the constant supervision of well trained special nurses. In order that direct relationships between changes in regimen and occurrence of seizures might be determined, each day was divided into four equal periods. One fourth of the diet, water and medication was given at the beginning of each six hour period. For the purpose of uniformity, the routine established was as follows: The patient, who was kept in bed under very light cover at all other times, was allowed up to use a commode placed at the bedside. The bladder was completely emptied at the end of each six hour period, after which the body weight without

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7. Johnston, M. W., and Newburg, L. H.: Determination of Total Heat Eliminated by the Human Being, J. Clin. Investigation **8**:147, 1930.

8. Newburg, L. H.; Johnston, M. W., and Falcon-Lesses, M.: Measurement of Total Water Exchange, J. Clin. Investigation **8**:161, 1930.

clothing was determined on an accurate balance sensitive to 5 Gm. The food, water and medication for the period were then given during the next hour. After the six hour urine collections were weighed, toluene and concentrated acetic acid were added as preservatives before samples were placed in the cold room. Feces were collected for the separate periods so far as possible by use of carmine demarcation. They were accurately weighed in the covered containers in which they were collected and were treated with 95 per cent ethyl alcohol before being dried over a steam bath. After being completely dried, they were reweighed in the same container, after which they were placed in air-tight sample bottles for storage in the cold room.

The water content of the urine and the foods was determined by weighing from 5 to 10 Gm. samples to the third decimal place before and after complete desiccation at reduced pressure over chemically pure sulphuric acid. Preliminary freezing with carbon dioxide snow was at first used, but this was later found to be an unnecessary refinement for the particular materials being dried. The fat content of the cream was determined by the well known Babcock method.[9] The nitrogen of all foods, urine and feces was determined by the standard Kjeldahl method.[9] Urinary chlorine was determined by the Volhardt method [9] and sulphur by the method of Fiske.[10] For the other mineral analyses samples of urine, stool and foods were first ashed by prolonged heating over a low flame with concentrated sulphuric and perchloric or nitric acids. The ashed materials were then diluted to appropriate concentrations with distilled water. For determination of the individual mineral elements, the following methods were used essentially as described: phosphorus and magnesium, by the method of Epperson [11] as adapted by Bassett, Elden and McCann; [12] sodium, by the method of Barber and Kolthoff; [13] potassium, by the method of Shohl and Bennett,[14] and calcium, by the method of Van Slyke and Sendroy.[15]

RESULTS

To conserve space and time the most important data have been condensed in graphic form on the accompanying charts, which are largely self-explanatory. They will now be briefly considered in their natural order.

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9. Hawk, P. B., and Bergeim, O.: Practical Physiological Chemistry, ed. 9, Philadelphia, P. Blakiston's Son & Co., 1926.

10. Fiske, C. H.: The Determination of Inorganic Sulfate, Total Sulfate, and Total Sulfur in Urine by the Benzidine Method, J. Biol. Chem. **47**:59, 1921.

11. Epperson, A. W.: The Pyrophosphate Method for the Determination of Magnesium and Phosphoric Anhydride, J. Am. Chem. Soc. **50**:2, 1928.

12. Bassett, S. H.; Elden, C. A., and McCann, W. S.: The Mineral Exchanges in Man: I. Organization of Metabolism Ward and Analytical Methods, J. Nutrition **4**:235, 1931.

13. Barber, H. H., and Kolthoff, I. M.: A Specific Reagent for the Rapid Gravimetric Determination of Sodium, J. Am. Chem. Soc. **50**:1625, 1928; Gravimetric Determination of Sodium by the Uranyl Zinc Acetate Method: II. Application in the Presence of Rubidium, Cesium, Potassium, Lithium, Phosphate or Arsenate, ibid. **51**:3233, 1929.

14. Shohl, A. T., and Bennett, H. B.: A Micro-Method for the Determination of Potassium as Iodoplatinate, J. Biol. Chem. **78**:643, 1928.

15. Van Slyke, D. D., and Sendroy, Julius: Gasometric Determination of Oxalic Acid and Calcium, and Its Application to Serum Analysis, J. Biol. Chem. **84**:217, 1929.

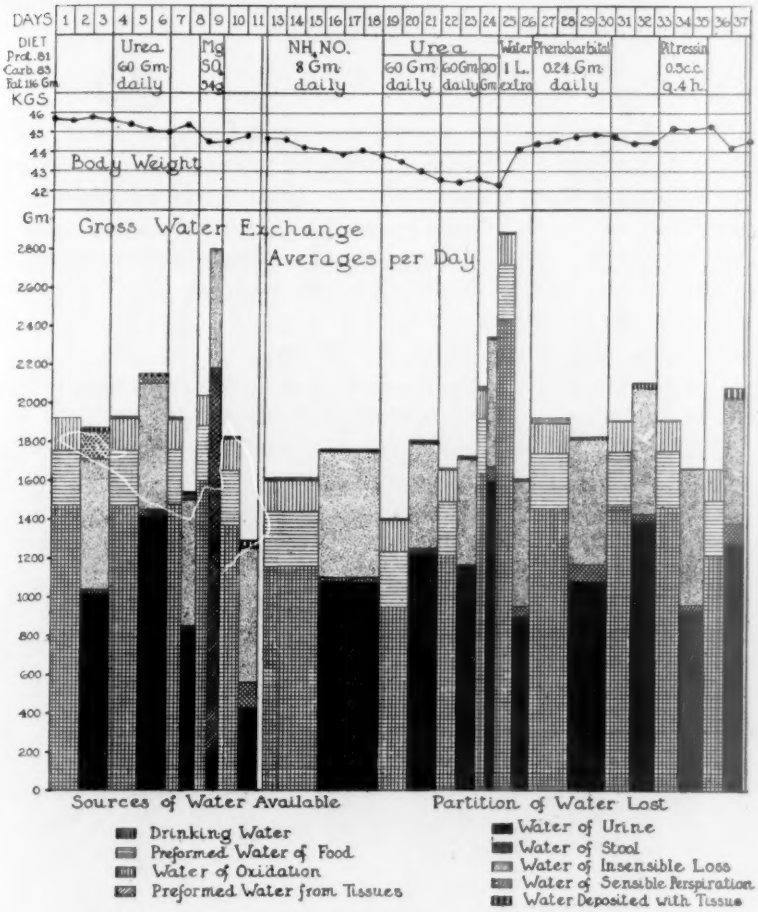

Chart 1.—Effects of various agents on the total water exchange of the body. The diet was constant throughout the entire study.

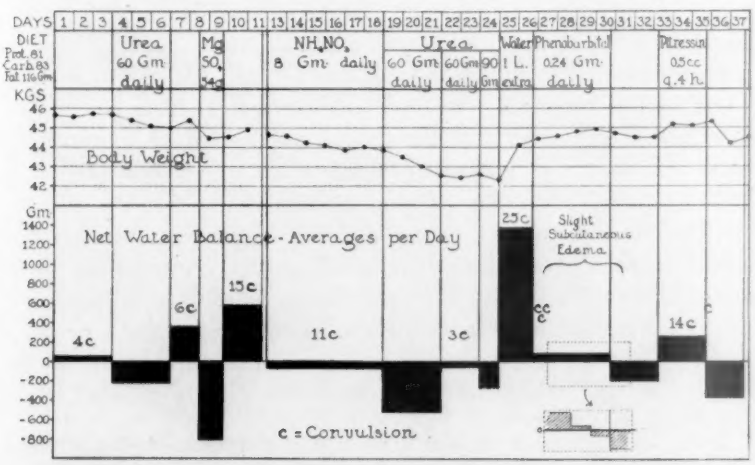

Chart 2.—Relationship of net water balance to occurrence of seizures. The inset during the period of phenobarbital administration shows the daily net balance instead of the average for the entire period.

Water Balances.—The complete data regarding the gross water exchange as measured during the successive experiments of the study are summarized in chart 1, while those showing the relationship between net balances and the occurrence of seizures are presented in chart 2. Because of the variation in length of the experimental periods, the values for each period are expressed as averages per diem.

In order that the values for the control period might be truly representative, the patient was fasted for one day and was then given the diet shown in the charts for an additional day before the data for the three day foreperiod recorded here were obtained. It is obvious that the patient was in normal water balance during this preliminary period, since thirst was entirely satisfied and there was even a slight gain in body water in spite of moderate visible perspiration. Four generalized convulsions occurred during this control period, a number definitely smaller, however, than average for this patient.

During the succeeding three days the experimental conditions were identical with those of the foreperiod except for the administration by mouth of 15 Gm. of pure urea every six hours for its diuretic effect. Urea was used for this purpose, because it is a normal body catabolite and is almost inert physiologically aside from its diuretic action. Its administration resulted in a gradual loss in body weight due to the development of a negative water balance of approximately 200 Gm. daily. No seizures occurred during the three days. When the urea was discontinued, however, partial rehydration resulted in six convulsions within the next thirty-six hours.

On the following day a markedly negative water balance was produced by the administration of 54 Gm. of magnesium sulphate (anhydrous). This was undoubtedly an excessive dosage. It is obvious that the water excretion was diverted from other routes to the alimentary canal in extreme measure. While there were no convulsive seizures during the thirty-six hours of active catharsis, it is apparent that the beneficial effect of the dehydration was short-lived. On partial rehydration, during the succeeding two days, there were fifteen severe convulsions, which suggested that the patient's condition, temporarily, not only was not improved, but was probably even worse than previously.

Following this rehydration period an attempt to test the effect of theobromine was made, but this was abandoned because sufficiently large doses to produce adequate diuresis caused vomiting. Ammonium nitrate, found by Keith, Whelan and Bannick [16] to be a desirable saline diuretic under certain conditions, was then given in full doses over a period of six days. Although it did not produce a small negative water balance after the first day, when the intake was also slightly reduced, eleven

16. Keith, N. M.; Whelan, M., and Bannick, E. G.: Diuretic Action of Nitrates and Their Use in Treatment of Dropsy, Tr. A. Am. Physicians **43**:288, 1928.

convulsions occurred during the six days. The time of these seizures is not shown in chart 2, but five of the eleven occurred in the early part of the period and four others on the fifth day when there was a slightly positive water balance.

A second period of urea administration was next included, differing from the first in that the water intake was varied. For the first three days, when the same quantity of urea, but 300 Gm. less water per day, was given, the magnitude of the negative water balance was more than double that of the first period. No seizures occurred during these three days, but the patient complained of considerable thirst. When the water intake was suddenly increased by 300 Gm. daily, the urea dosage remaining unchanged, the size of the negative balance was greatly diminished. With the partial rehydration, which took place on the second day, the patient had three mild convulsions. When the water intake was still further increased to a level 50 per cent above that in the previous three day period but was accompanied by an increase of 50 per cent in the urea dosage, a negative water balance of intermediate magnitude was produced and no seizures occurred. These results indicate that there is no fixed level of total water exchange above which seizures will occur regardless of other conditions and below which they will not occur. The net balance would appear to be of far greater significance.

Since the patient had now lost a considerable amount of weight, due largely to water loss, it was decided to discontinue administration of urea and give her all of the distilled water that she wished to drink. Within the first twelve hours on this regimen, she drank 1 liter in excess of that allowed in the original control period. In spite of the fact that she had been on a low sodium chloride intake for a period of over twenty-five days and had shown a deficit of this salt in each period of diuresis, the patient stored approximately 1,500 Gm. of water in one and three-fourths days. Within fifteen hours after consumption of the extra water, she began to have severe generalized seizures at frequent intervals. She had twenty-eight convulsions within two days.

Phenobarbital was then given every six hours in almost maximal doses over a period of four days. Although the patient continued to store water at a diminishing rate during the first three days of phenobarbital therapy, no convulsions occurred after the first twelve hours of this period. In spite of the fact that the urine contained no albumin or casts and the heart action apparently remained normal, slight but definite puffiness of the face and pitting edema over the legs appeared. On the fourth day there was a slightly negative water balance, as shown in chart 2. After withdrawal of the phenobarbital a negative balance of even greater size persisted over a period of two and one-half days. There were no seizures during this time. However, this negative balance was quickly terminated, and a positive balance of equal magnitude

was again established by the administration of a potent antidiuretic extract of the hypophysis cerebri (pitressin, Parke, Davis & Co.). After thirty-six hours of positive balance a convulsion occurred, which was followed by fourteen more within the next twenty-four hours.

When the administration of pitressin was discontinued, and the water intake was slightly diminished, a large negative water balance developed and the convulsions ceased to occur rather promptly. After termination of the study this patient was placed on a strict dietary regimen, consisting of a borderline, nonketogenic diet and moderate restriction of her total water intake. On this regimen she remained free from seizures for more than one month, but on breaking the diet, again returned to her previous state.

Comment on Water Balance.—The correlation between positive water balance and the occurrence of seizures in the case of the severely epileptic patient under the special conditions of these experiments is obvious from charts 1 and 2. Differences in body weight during the various subperiods were undoubtedly due almost entirely to differences in the amounts of water contained in the body. That there was no significant decrease in the quantity of body protein is demonstrated by the fact that the nitrogen and sulphur balances were maintained practically throughout the study as in the control period. Slightly positive balances for calcium and phosphorus indicate that there could have been no destruction of bone. Figures on the total energy metabolism preclude the possibility that the weight losses could have been due to catabolism of stored fat. In fact, there tended to be storage of small amounts of fat during most of the periods. The various sources of the water lost will be considered in the comments on the mineral balances.

Contrary to what might on first thought be expected, there was apparently no less tendency for seizures to follow the establishment of a positive water balance after the total volume of body water had been reduced by 2 or 3 Kg. than at the beginning. In fact, if there was any change at all in the ease with which seizures could be induced, it was in the direction of being increased. We have often observed this same tendency in other persons with severe epilepsy under the therapeutic water restriction regimen, especially during the first weeks. It appears that the total volume of water passing through the body in a given period is less significant than the net balance. The length of time that it is retained, its final location and the physical state in which it is held are undoubtedly significant factors. A large volume of water may apparently be taken with impunity, if it is promptly excreted. Furthermore, a large excess of extracellular or interstitial isotonic fluid may exist in the tissues outside of the brain or there may even be a certain degree of this type of edema of the brain tissue itself without great

harm, but even a small excess of water within the brain cells would probably disturb the ionic and colloidal equilibria to the extent of markedly increasing irritability. Full knowledge regarding the translocation of water in the body from the twenty-fifth day on in the present study would probably be of inestimable value for the solution of our problem. The sudden ingestion of a large volume of water by a patient who has undergone successive periods of negative balance for a fortnight would be expected to tax her mechanism for controlling mineral and water exchanges almost to the limit. Sustained pituitary antidiuresis with moderate or greatly increased water intake should do the same and so defects in these mechanisms might be expected to manifest themselves under these special strains. The specific effect on these processes of a sedative, such as phenobarbital, may be of especial importance. Does it in any way influence the translocation of water in the body or determine the physical state or the chemical associations in which it is held? What change occurs in the cells during the course of spontaneous water loss, such as that observed following the periods when phenobarbital and pitressin were administered, to favor cessation of convulsions? These are fundamental questions. That factors other than the gross water content of the body must be discovered to account for the convulsive reactions is clearly evident from a comparison of conditions during the various experiments. Fortunately, we have at hand data on the mineral exchanges for these periods, which carry us one step further.

Mineral Balances.—Because of the intimate relationship of water and mineral metabolism any consideration of either alone is incomplete. In fact, as regards such phenomena as irritability, which concerns us so greatly in the present study, the interplay or balance between the electrolytes is probably the factor of chief importance. Charts 3 and 4 have been constructed to present the data regarding the total mineral balances for the successive periods as described in discussion of the water balances. In the later charts significant data are presented for twelve hour periods.

Figures for the average per diem intake and total output of sodium, potassium, magnesium and calcium are shown for the successive periods in chart 3. It is seen that calcium was being stored throughout the entire period of study except during the period of saline catharsis. It is obvious that by far the larger portion of the calcium output was by way of the feces. The urinary calcium rose to its highest level during the period of ammonium nitrate administration. This is perhaps best explained as a secondary effect of the acid-forming salt on the acid-base equilibrium of the body. Unfortunately, there is no satisfactory method of obtaining representative samples of feces for short

periods, which would be required for accurate balance studies of this important element and of magnesium.

The latter substance, about 50 per cent of which was lost by way of feces, showed somewhat more variabilty than did calcium. It tended to follow the excretion-curve of potassium more closely than that of either calcium or sodium, although this tendency was apparently not carried sufficiently far to be of certain significance. Since the excess

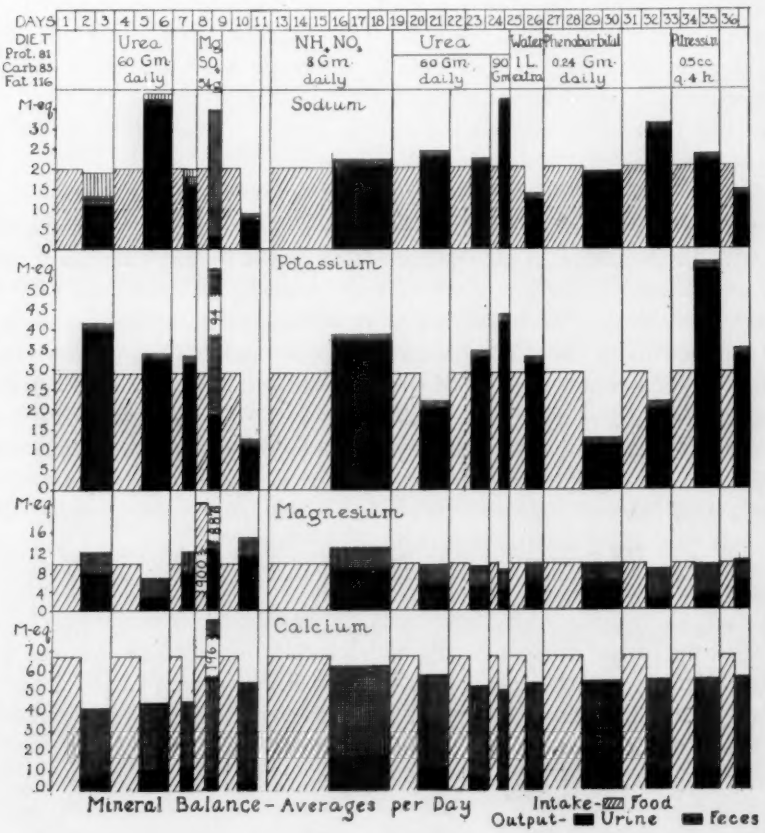
DAYS 1 2 3 4 5 6 7 8 9 10 11 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36
DIET
Prot. 81
Carb 85
Fat 116
Urea 60 Gm. daily
Mg SO4 24 g
NH4NO3 8 Gm. daily
Urea 60 Gm. daily
90 Gm.
Water 1 L. extra
Phenobarbital 0.24 Gm. daily
Pitressin .05cc q. 4 h.
M-eq
Sodium
Potassium
Magnesium
Calcium
Mineral Balance - Averages per Day
Intake - Food
Output - Urine
Feces

Chart 3.—Average daily intake and output of the four important metallic elements, showing their partition between the urine and stool. Potassium and sodium showed the greatest amount of variation. The calculated sodium in the sensible sweat is represented by parallel perpendicular lines.

given as magnesium sulphate during the fourth period was excreted by the end of the fifth period, the negative balance of approximately 3 milliequivalents per day during the six day period of ammonium nitrate administration is undoubtedly of some significance. That at least a small amount of the ingested magnesium sulphate was absorbed during

the period of severe catharsis is evident from the fact that the total urinary excretion of magnesium, and of sulphur as well, was increased in spite of the fact that the volume of urine was reduced almost to a minimum. Of course, the absolute amount appearing in the urine was extremely small, considering the total amounts ingested and lost by way of the bowel. Apparently urea diuresis had no important effect on either magnesium or calcium excretion. Nor were the exchanges of

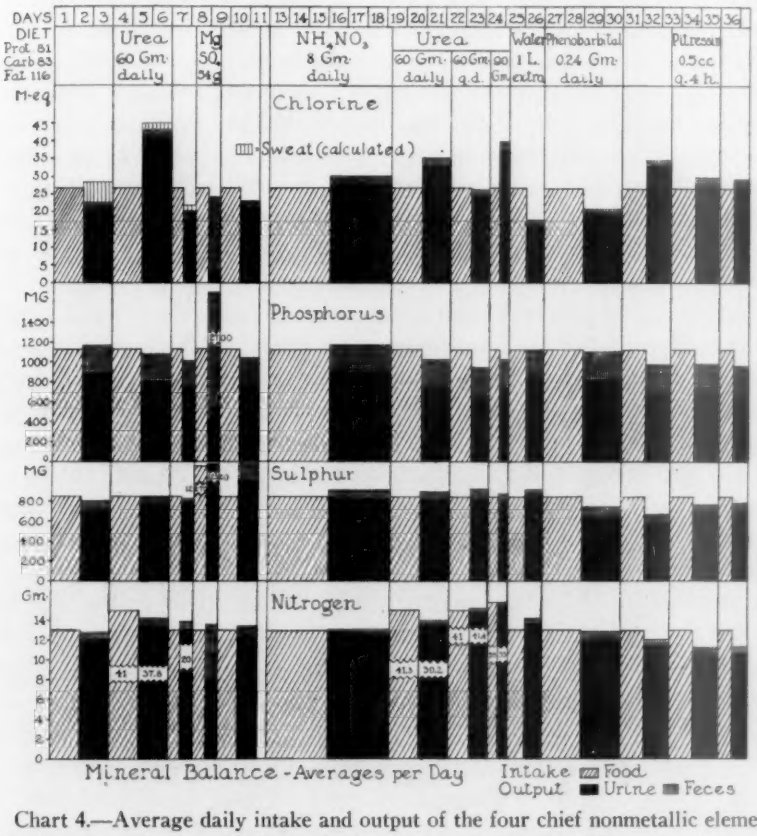

Chart 4.—Average daily intake and output of the four chief nonmetallic elements. Chlorine alone shows a fairly marked variation during the different periods.

these elements influenced to any demonstrable degree by forced water drinking or by administration of phenobarbital or pitressin.

Potassium showed more frequent and wider fluctuations than any of the other elements studied, with sodium taking a second place. During the three day foreperiod there was a strongly negative potassium balance, whereas the sodium balance was apparently slightly positive. The wider difference here can be explained in part only by the fact that more sodium than potassium is lost in the sensible perspiration.

When the calculated amount of sodium so lost (6 milliequivalents, considering sweat to contain 0.2 per cent sodium chloride) is added to that excreted by way of the urine and feces, the ratio of potassium to sodium milliequivalents is still 2.2 : 1, without taking into account the potassium in the perspiration, whereas the intake ratio has a value of less than 1.5 : 1. During the following three day period of urea administration, while there was still a slightly negative potassium balance, the absolute amount excreted per day was less than during the previous period. The sodium excretion, on the other hand, was greatly increased by the diuresis, giving a value for the potassium-sodium ratio of 0.9 : 1. With discontinuance of the urea, sodium balance was again restored, while the potassium loss continued. The magnesium sulphate catharsis produced a much larger loss of potassium than of sodium. As would be expected, all mineral as well as water excretion was diverted from the urinary to the enteral pathway. The stool showed a potassium-sodium value of 3 : 1. During the period of rehydration following discontinuance of the cathartic, partial remineralization also occurred.

For the period of ammonium nitrate adminstration there was a negative potassium balance of moderate size, while the sodium loss was extremely slight, giving a potassium-sodium ratio of 1.5 : 1. Following a slight reduction of the water intake and the substitution of urea for ammonium nitrate, potassium was stored, while sodium showed a net loss. When, however, the water intake was increased 20 per cent without changing the urea dosage, the preponderance of potassium excretion again appeared. With an increase of 50 per cent in both water intake and urea dosage, the output of both potassium and sodium was moderately increased. With the sudden administration of an extra liter of water in the next period, sodium was stored with water while potassium was lost. The probable significance of these variations will be brought out in connection with other charts.

The effects of phenobarbital under the unusual conditions of this experiment are of special interest because of the specific therapeutic action of this drug in epilepsy. The most striking effect was that of causing a large storage of potassium, an amount in fact more than twice that lost during the three preceding periods together. A very small quantity of sodium was likewise stored. While the positive balance of potassium continued throughout most of the succeeding period, the sodium excretion exceeded the intake. Since chlorine likewise showed a considerable net loss, it appears most likely that the negative water balance was due to loss of extracellular body fluid.

In spite of the storage of over a liter of water during the period of pituitary antidiuresis, there was an extensive loss of body potassium and a very slight loss of sodium as well. The possible significance of

the potassium loss under these conditions will be considered under the general discussion. During the short period following pitressin administration there was a definite retention of sodium, whereas moderate amounts of potassium were lost in the excess water eliminated in the urine.

Data regarding the nonmetallic elements for the various periods are condensed in chart 4. A comparison of the values for chlorine with those for all of the other elements shows that they correspond most closely with those of sodium on the whole. There is no such close parallelism with potassium except during the last two periods. There does not appear to be any definite relationship with calcium or magnesium. Except for a fairly great loss during the period of magnesium sulphate catharsis, phosphorus appears to have remained essentially in balance as shown by the average figures for entire periods. It is probable that determinations for shorter periods would show significant variations in relation to the convulsions.

With the exception of the changes incident to the period of magnesium sulphate catharsis, sulphur showed no important variations in either short or long periods, being unaffected by other procedures or by seizures. The inorganic fraction of the urinary sulphur was determined as well as the total sulphur. Contrary to the claim of Kauffmann,[17] that the unoxidized form constitutes the major fraction of urinary sulphur in the epileptic subject, the values for the various fractions showed that the partition was normal at all times throughout this study.

Figures for the nitrogen exchange are of importance chiefly in indicating that little or no body protein was lost during the experiments. The data regarding sulphur tend to substantiate this conclusion. Apparently all but a small fraction of the urea ingested was finally accounted for, although there was a short lag in its excretion. It is evident that the convulsions occurring in various periods, like voluntary muscular work, have little or no direct effect on nitrogenous metabolism.

The foregoing charts with brief explanatory notes present only the general correlations between changes in the water and mineral balances on the one hand, and the occurrence of convulsive seizures on the other. On the four remaining charts significant data for twelve hour periods are given to show what appear to be more specific relationships of the convulsions to changes in the mineral metabolism as reflected in the urinary sodium, potassium and chlorine. Unfortunately such data cannot be satisfactorily obtained for calcium and magnesium because of the difficulty of collecting the feces in short periods. The sodium, potassium and chlorine were determined in representative

17. Kauffmann, M.: Beiträge zur Pathologie des Stoffwechsels bei Psychosen: II. Die Epilepsie, Jena, G. Fischer, 1908.

twelve hour periods for all of the experiments, excepting those in which magnesium sulphate and ammonium nitrate were given. In the charts the urinary water is given in grams, while the sodium, potassium and chlorine are expressed in milliequivalents, which together present a graphic picture of the solution lost from the body in each night and day period.

Chart 5 shows the last day of the original control period, the entire three days of the first period of urea administration and the first day of the succeeding rehydration period. The striking features regarding these data are the tendency toward similarity between the first and third periods and the contrast between these on the one hand and that of the

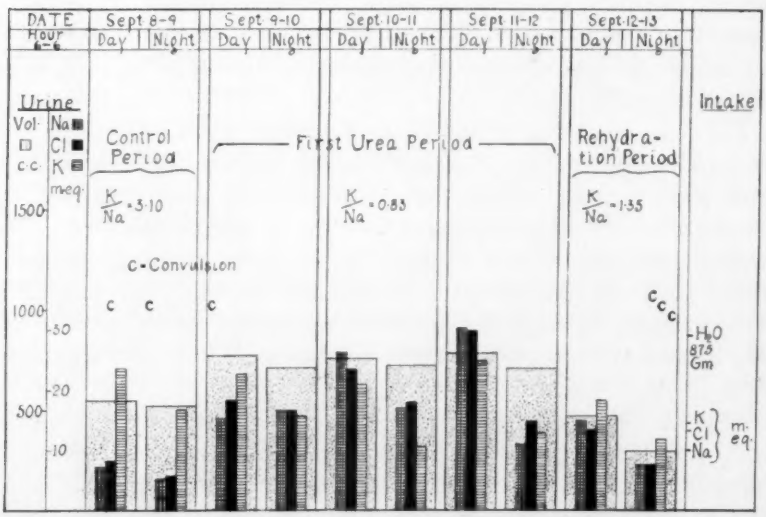

Chart 5.—Effects of urea diuresis on urinary mineral content in relation to occurrence of convulsions. Increase in ratio of potassium to sodium preceded onset of seizures in rehydration period.

period of urea administration on the other. On the third day of the three day foreperiod, the amounts of sodium and chlorine excreted were well below the intake, whereas the potassium balance was strongly negative, giving a potassium-sodium value of 3.1 : 1. Because twelve hour determinations for the previous two days were not made, it cannot be said whether the excess of potassium appeared in the urine before the convulsions began or not. However, in the rehydration period it appears that this was the case, an observation, which, if correct, may be of considerable significance. After the first twelve hours of the period of urea administration, when the proportions of the various elements remain similar to the foregoing, the output of sodium and

chlorine increased between 300 and 400 per cent, while the potassium averaged approximately the same, giving a potassium-sodium value of 0.83 : 1.

Chart 6 shows data for the second period of urea administration with its three subdivisions and for the following rehydration period. This chart shows clearly the effect of additions of water to the regimen. When the data for the last thirty-six hours of the first subperiod (1,400 Gm. of water and 60 Gm. of urea given) are compared with those of the corresponding part of the second subperiod (300 Gm. additional water per day), it is seen that the chief difference is due to an absolute and relative increase in the amount of potassium excreted.

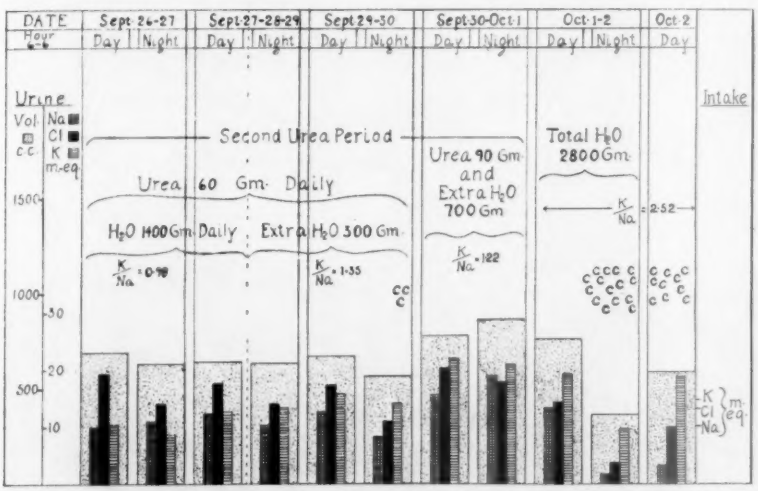

Chart 6.—Effects of increasing water intake on mineral excretion and occurrence of convulsions. The increase in the potassium and sodium ratio preceded the onset of seizures.

Here again it is obvious that this change manifested itself before the convulsions occurred. The ratio of potassium to sodium expressed in milliequivalents was increased from 0.98 : 1 to 1.35 : 1. During the third subperiod of the second general experiment with urea (both water and urea increased 50 per cent), excretion of all three elements rose. Although the average potassium-sodium value was 1.22 : 1, no seizures occurred. The degree of dehydration reached its maximum for the entire study on this day. The next experiment was undoubtedly one of the most important of the entire series, because the attempt to restore a large part of the previously lost body water within a short space of time resulted in the patient's having twenty-eight severe convulsions in the course of thirty-six hours. With the subsidence of the

urea diuresis and the storage of water in the body, the elimination of sodium and chlorine fell to a very low level, while the potassium excretion remained relatively high, again giving a high potassium-sodium value, 2.52 : 1. It appears here as in the two previous instances that the ratio had increased before the seizures occurred.

Data for the entire period of phenobarbital administration and for the first thirty-six hours of a sixty hour control period are graphically shown on chart 7. The absolute quantity of mineral being excreted during the first half of the period of phenobarbital administration, when water was still being stored, was very small indeed. After the first twelve hours of phenobarbital administration, seizures ceased to occur and the excretion of both sodium and chlorine came to exceed that of

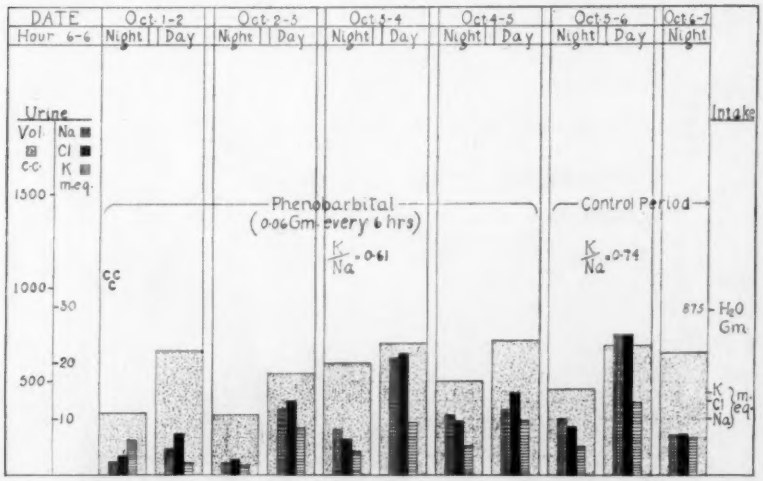

Chart 7.—Effects of phenobarbital therapy on mineral and water balance. Storage of minerals and water during first two and one-half days. Potassium storage marked throughout period.

potassium, so that the potassium-sodium ratio for the entire period was 0.61 : 1. Since the ratio of potassium to sodium in the diet was only slightly less than 1.5 : 1, the values shown, even after stored water began to be excreted, indicated an active storage of potassium with sodium practically in normal balance. During the control period following phenobarbital administration this same tendency continued up to the last day in spite of the fact that sodium and chlorine were again being lost with the diuresis that developed spontaneously. It should be noted that the potassium-sodium ratio for this period was 0.74 : 1, and that no convulsions occurred.

The last twenty-four hours of the control period following phenobarbital administration, the entire pituitary antidiuresis period and the

first twenty-four hours of the postantidiuresis period are represented in chart 8. It is obvious that the potassium was not only not being stored during the last day of the period following phenobarbital administration but was again in negative balance. During the night twelve hour period, the potassium excretion exceeded the sodium and chlorine considerably for the first time since the beginning of the phenobarbital period. With the establishment of pituitary antidiuresis the excretion of potassium increased to a level over 50 per cent above the maximum of any other experiment in the series and over 100 per cent above the intake. This excessive loss of potassium continued unabated throughout the period of pitressin administration and showed some overlapping into

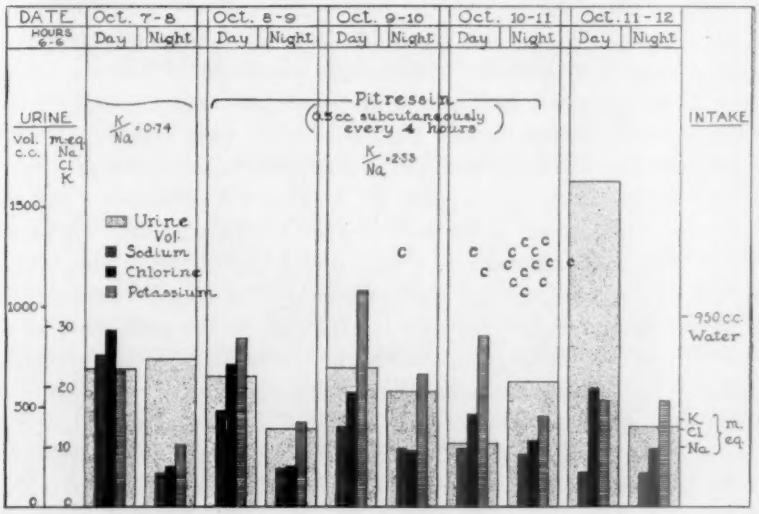

Chart 8.—Effects of sustained pituitary antidiuresis on water and mineral exchange. Markedly negative potassium balance appeared thirty-six hours before onset of seizures.

the next period when the stored water was being excreted. The sodium remained practically in even balance during the antidiuresis period but was stored during the after period. Chlorine showed a slightly negative balance for the period. It is again very evident that the excessive potassium excretion in the period of sustained antidiuresis began long before the first seizure occurred.

Comment on Mineral Balance.—The most striking feature of this series of experiments as regards the mineral exchange was the variation in the composition of the urine during the different periods in spite of a constant diet. During periods characterized by the development of positive water balances and the occurrence of convulsive seizures, the excretion of potassium greatly exceeded that of sodium. Were one to

look alone at charts 3 and 4, which give total averages for entire periods, one would probably be justified in assuming, as we at first did, that the extra potassium was eliminated solely to meet the need for excretion of the excess of acid produced in the body by the convulsions. However, inspection of the last four charts reveals the fact that the relative increase in potassium excretion apparently began before the first seizure occurred. Since most of the potassium in the human body is held within the cells behind cell membranes, which are ordinarily but slightly permeable to this element, its loss during periods when water was being stored, particularly during the period of pitressin administration, indicates an actual "leakage" from the cells at such times. Assuming that the kidney function is entirely normal, the most plausible explanation for the rise in potassium excretion some time before the occurrence of seizures is that the permeability of the cell membranes to this element was temporarily increased. During the course of a previous experimental study on the acid-base equilibrium,[18] the subject of the present experiments repeatedly showed a distinct shift of the plasma p_H toward the alkaline side prior to the onset of seizures in accordance with earlier findings by Jarløv [19] and Geyelin, Bigwood and Wheatley.[20] In retrospect, that observation may now find an explanation in the present results. The fact that certain other patients did not show this shift in p_H serves as a warning that the preliminary potassium "leakage" may not be demonstrable in every case. Inasmuch as the urine volume was actually much smaller during the various periods of water storage and relatively high potassium excretion, the possibility of explaining the latter phenomenon on the basis of "flushing" is eliminated. During the periods of active diuresis which were interspersed between the convulsive periods, however, there may well have been a flooding out of any potassium that had accumulated in the extracellular fluids.

During periods when no seizures occurred, the urinary sodium exceeded the potassium. During every period of active diuresis, excepting that following the discontinuation of pitressin, the excretion of sodium was greatly augmented. The chlorine output was usually intermediate, as might be expected from the facts that it easily combines with both bases and occurs as an important anion within as well as outside of the cells of the body.

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18. McQuarrie, Irvine; and Keith, H. M.: Experimental Study of the Acid-Base Equilibrium in Children with Idiopathic Epilepsy, Am. J. Dis. Child. **37**:261 (Feb.) 1929.

19. Jarløv, E.: Sur l'équilibre acido-basique du sang humain étudié dans ses rapports avec diverses affections, Compt. rend. Soc. de biol. **84**:156, 1921.

20. Geyelin, H. R.; Bigwood, E. J., and Wheatley, M. A.: The Reaction of the Blood in Epilepsy, Proc. Soc. Exper. Biol. & Med. **21**:227, 1923.

The two periods of greatest interest are those in which phenobarbital and pitressin were administered because the contrast in the urinary data was striking. In both periods there was a positive water balance, but no seizures followed the water storage in the period of phenobarbital administration. In this instance visible and palpable subcutaneous edema appeared on the second day, coincidently with the cessation of seizures and the storage of both minerals and water. The urinary potassium-sodium value (0.61 : 1) reached the lowest level attained during the entire course of the study. The subcutaneous edema remained in evidence for several days until removed by spontaneous diuresis during the period following phenobarbital administration. The fact that sodium and chlorine were the predominating mineral elements of the urine during this after-period indicated that the additional water eliminated had an extracellular origin.

In striking contrast to this there was no demonstrable edema during the pituitary antidiuresis period in spite of a slightly greater water retention than during the period of phenobarbital administration. Instead of mineral storage there was mineral loss. The increase in potassium excretion was particularly marked, resulting in a potassium to sodium ratio of 2.33:1. Since the elimination of extra potassium began at least thirty-six hours before the first of the fourteen convulsions occurred, it cannot be accounted for as a result of the convulsions. It appears to us far more likely that the convulsions resulted from some disturbance in the cell physiology involving the water and electrolyte relationships. These results and data, reported elsewhere,[21] indicate that pituitary antidiuresis tends to aggravate the abnormal state already present in the epileptic subject.

The site of water storage during the period of pitressin administration and during the other periods, in which convulsions followed the establishment of a positive water balance, is problematic. The physical or chemical state in which it was held may have differed from that of the period of phenobarbital administration, although there was no definite evidence of this aside from the absence of edema. The two facts, that subcutaneous edema could not be demonstrated and that the composition of the urine during the diuresis period following pitressin administration was characterized by a low sodium and a high potassium content, indicate that much of the water may have been stored within fixed cells and on leaving them carried potassium with it. An alternative interpretation is that all of the extra water was stored extracellularly and contained potassium, which had diffused into it from the cells during the period of antidiuresis. While there is no definite evidence to prove which interpretation

21. McQuarrie, Irvine; and Peeler, D. B.: Effects of Sustained Pituitary Antidiuresis and Forced Water Drinking in Epileptic Children, J. Clin. Investigation **10**:915, 1931.

is the more nearly correct, the lack of edema suggests the probability that at least some of the water entered the cells when the osmotic pressure of the extracellular fluid was reduced, especially during the period of pitressin administration. It seems possible that phenobarbital may have effected a translocation of water from the intracellular to the extracellular reservoirs and at the same time directly or indirectly caused a restoration of the normal relationships between the electrolytes, whereas pitressin antidiuresis or a sudden increase in the water intake appears to have had the reverse effect. Further work on this particular question is now in progress.

The chain of abnormal events repeatedly witnessed after the establishment of a positive water balance could be explained most easily on the assumption that it had its beginning in an abnormal passage of water into the brain cells. In such an event secondary changes of a grave character would be expected to occur from dilution of the cell contents, such as imbibition of extra water by the cell colloids (particularly lipids and proteins), diminution in their adsorption capacity for electrolytes and other disturbances in the interrelationships of the various chemical systems determining the physiologic activities of the cells. That potassium ions migrate from the cells under these conditions is almost certain. Whether sodium ions found freer entry to the cells than under normal conditions, we cannot say, because there is no suggestion of this during any of the periods under discussion with the possible exception of that following the ingestion of an excessive amount of water. Shifts of the other elements may be of importance, but so far we have no reliable evidence regarding them during short periods. Determination of the major mineral constituents of the blood under experimental conditions similar to those in the present study are contemplated with the hope that additional information might be obtained.

From our present data it is impossible to tell what particular organs participated in the loss of potassium during the periods of negative potassium balance. Since epilepsy is assumed by most authorities to be a disease primarily of the nervous system, it is entirely natural to suppose that the potassium lost before the onset of seizures came chiefly from the brain and other nerve tissue, in which event it would probably indicate a defect in the cells' mechanism for retaining it. Inasmuch as excitation is known to increase cell membrane permeability, it might be expected that potassium would be lost from the muscles, and possibly from other tissues as well, during the convulsive periods. Prolonged stimulation of the sciatic nerve has been found experimentally to reduce the potassium content of the muscles of the leg.[22] It appears to us that

22. Harrison, T. R.; Calhoun, J. A.; Cullen, G. E., and Pilcher, C.: The Relation of Edema and of Fatigue to the Potassium Content of Skeletal and Cardiac Muscle, J. Clin. Investigation **9**:8, 1931.

the extra potassium lost in the feces during the magnesium sulphate catharsis period may have been derived primarily from the cells of the gastro-intestinal mucosa. We are well aware of the fact, however, that all of these statements regarding the possible sources of the potassium are highly conjectural.

COMMENT

If we may assume that the data regarding the water and mineral exchanges in the case of this severely epileptic child are representative of the variations occurring under similar conditions in the group of epileptic patients known to be sensitive to alterations in water balance, we may have here a partial explanation of the mechanism by which water storage appears to favor the occurrence of seizures. While the results presented must necessarily be interpreted strictly within the limits of the special conditions of our experiments, they appear to us to furnish new suggestions regarding the nature of the physicochemical pathology of genuine epilepsy. It must be frankly recognized, of course, that not all patients with the diagnosis of "epilepsy" fall into the same etiologic classification and so cannot all be expected to react in the same way.

That this unique convulsive disorder has its origin in some abnormality of the brain that is not detectable by ordinary histologic technic was the final conviction of a number of the older authorities on the subject, particularly Kussmaul and Tenner [23] and Gowers.[24] The latter especially emphasized the belief that the characteristic convulsive tendency is due to some innate abnormality in the brain cells as a whole rather than to a single lesion in any particular portion of the brain. While he ventured interesting suggestions regarding the possible nature of the supposed functional disturbance, he frankly admitted their inadequacies and expressed the opinion that final solution of the problem must await further advances in brain physiology. A number of recent workers in the field have adopted the same general point of view.[25]

The numerous theories that have been advanced regarding the etiology of epilepsy have been subjected to a critical review by Lennox and Cobb [26] and so need not be considered here. It is sufficient to say

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23. Kussmaul, A., and Tenner, A.: Epileptiform Convulsions Caused by Profuse Bleeding and Also True Epilepsy, translated by E. Bronner, New Sydenham Society, London, 1859; quoted by Lennox and Cobb.

24. Gowers, W. R.: Epilepsy and Other Chronic Convulsive Diseases, London, J. & A. Churchill, 1881.

25. Bisgaard, A.; Jarløv, E., and Nørvig, J.: Undersøgelser over neutralitetsregulationen ved geniun epilepsi, Hospitalstid. **61**:960, 1918. Lennox, W. G., and Cobb, Stanley: Epilepsy from the Standpoint of Physiology and Treatment, Medicine **7**:105, 1928. Georgi, F.: Pathogenesis of Epileptic Seizure, Deutsche Ztschr. f. Nervenh. **89**:126, 1926.

26. Lennox and Cobb (footnote 25).

that after an unbiased survey of the literature and a careful analysis of their own extensive data, these authors were forced to conjecture that some obscure chronic disturbance in the physiologic reactions involving the brain, such as may result for instance from spasmodic contraction of the cerebral arteries, is etiologically responsible for the syndrome of epilepsy. After briefly discussing some of the factors that are known to influence its clinical course temporarily, they said:

> The physiological changes which we have mentioned (anoxemia, alkalosis and edema) are themselves only contributing factors. They tend to induce seizures by increasing irritability of nervous tissues, producing an effect which is not specific for epilepsy. Induction of acidosis is a useful therapeutic measure not only in certain cases of epilepsy, but also in other paroxysmal manifestations such as muscle cramps, hiccough and tetany. Furthermore, the physiological changes mentioned will produce seizures only in those who are subject to seizures. Therefore, the important question yet remains, why under a given stimulus, one person should have a seizure and another not. . . . As we have emphasized above, there is no constant anatomical lesion in epilepsy, and only a minority of patients with extensive cerebral pathology have fits. We are forced then to postulate some unknown constitutional element. This abnormal convulsive capacity is presumably present in some degree in each person with epilepsy.

This paragraph is quoted because it is a concise and authoritative statement of the real problem and clears the way for the tentative interpretation which our present results and other data recently obtained appear to require. We find ourselves in full agreement with the spirit of their assertion that, "what is needed is not more theories but more facts," for the solution of the epilepsy problem. Nevertheless, the experimental data that have been obtained during recent years do not seem to us to find satisfactory explanation in any single generalization so far expressed. We have become somewhat intrigued by the hope that more definite information regarding the "unknown constitutional element" responsible for the abnormal "convulsive capacity" or "reactivity" of the epileptic patient might be obtained. Recently obtained experimental data of three different kinds, requiring a common interpretation, have suggested the possibility that the epileptic differs from the normal subject in having an inherent deficiency in his mechanism for regulating the semipermeability of the brain cell membranes. The possible relationship of increased cell membrane permeability to the occurrence of seizures was first indicated by the finding with Bloor and Patterson [27] that they tend to be associated with an increase in the ratio of lecithin to cholesterol in the blood plasma. Since there can be very little doubt that epilepsy is primarily a disease of the brain, an organ

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27. McQuarrie, I.; Bloor, W. R.; Patterson, H. A., and Husted, C.: The Possible Significance of Changes in the Blood Lipids in Epilepsy, Am. J. Dis. Child. **42**:720 (Sept.) 1931.

preeminently rich in these lipid substances, the blood changes were tentatively interpreted as being an index to alterations in the brain cells. The special rôle of these substances in controlling permeability of cell membranes in general has received consideration particularly in connection with various theories of narcosis and irritability.[28]

The findings described in the present paper constitute the second line of indirect evidence of disturbed permeability of cell membranes during what may be called the active phase of the disease. The possible abnormal entry of water into the cells and the apparent "leakage" of potassium prior to the onset of seizures in our experiments finds analogies in the observation of MacDonald [29] that nerve tissue placed in a simple isotonic solution such as Ringer's undergoes swelling and loses potassium by diffusion at points where it is stimulated or injured. It is an accepted fact that membrane permeability is increased by excitation or injury.[30]

A third source of indirect evidence suggesting that the barriers against injurious interchanges of water and electrolytes are characteristically defective in this disease is that found from a recent research on the effects of sustained pituitary antidiuresis in mildly epileptic and normal children by McQuarrie and Peeler.[21] It was found by that investigation that convulsions could be induced at will in the mildly epileptic but not in the nonepileptic subjects by forcing the establishment of a positive water balance of a certain magnitude. Preliminary dilution of the extracellular body fluids appeared to be a prerequisite for the provocation of seizures since administration of just sufficient sodium chloride to prevent such dilution tended to prevent them in the particular patients studied. Inasmuch as other possible factors, such as increase in the intracranial pressure and the vasopressor action of the pituitary extract, were practically ruled out as causes of the seizures, the third alternative was that with the lowering of the osmotic pressure of the extracellular fluid which resulted from the procedure, water entered the

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28. Leathes, J. B.: Rôle of Fats in Vital Phenomena, Lancet **1**:803, 853, 957 and 1019, 1925. Lillie, R. S.: Protoplasmic Action and Nervous Action, Chicago, Chicago University Press, 1923. Winterstem, H.: Die Narkose, ed. 2, Berlin, Julius Springer, 1926. Höber, R.: Physicalische Chemie Zelle und der Gewebe, ed. 5, Leipzig, Wilhelm Engelmann, 1924.

29. MacDonald, J. A.: Migration of Potassium and the Injury Current, J. Physiol. **32**:66, 1905.

30. Bayliss, W. M.: Principles of General Physiology, ed. 4, New York, Longmans, Green & Co., 1924. Syz, H. C.: On the Entrance of Convulsant Dyes into Substance of the Brain and Spinal Cord After Injury to These Structures, J. Pharmacol. & Exper. Therap. **21**:263, 1923; Observations on Experimental Convulsions with Special Reference to Permeability Changes, Am. J. Psychiat. **7**:209, 1927.

cells of the brain and probably electrolytes diffused from them as during the period of pitressin administration in the present study.

The findings by Lennox and Cobb [26] that alkalosis and anoxemia from reduced oxygen tension or vascular spasm both favor the occurrence of convulsions in epilepsy are compatible with our tentative interpretation, because both of these factors are known to increase cell membrane permeability.[31] Emotional excitation, which has long been recognized as a contributing factor in the provocation of seizures, probably has an effect on the cell membrane similar to that of other forms of stimulation. As pointed out by Bayliss,[32] the ease with which substances important to the life of the cell pass through its membranes undoubtedly varies continuously throughout the day with changes in physiologic activity. The great variability in the convulsive reactivity of an individual epileptic patient from one time to another may well be dependent in part on abnormal accentuations of these natural variations. It appears reasonable to us, on the other hand, that the long remissions or spontaneous "cures" occasionally experienced may depend on favorable alterations in the mechanisms regulating permeability. It is especially significant that the substances which prevent seizures, namely, the anesthetics, narcotics and sedatives, are also those which apparently decrease cell membrane permeability.[33] The possible effects on this function of the cell of other factors therapeutically important in epilepsy, such as dehydration, acidosis, fasting, the ketogenic diet and bromides, will be considered in subsequent papers.

Regarding the possible nature of the mechanism determining the physiologic behavior of the nerve cell membranes, little definite information is available. The finding of changes in the plasma lipids suggests the possibility that the chemical structure of the cells themselves may be at fault. Comparative analyses of normal and epileptic brains for water, minerals and lipids are contemplated to test this possibility. That this is a promising undertaking is also suggested by the fact that during childhood, a period characterized by an increased susceptibility to convulsions, the water content of the brain is normally much higher and the cholesterol content much lower than during later life. A second possibility is that there is an as yet undiscovered central nervous or hormonal mechanism for regulating this important vegetative function,

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31. Landis, E. M.: Micro-Injection Studies of Capillary Permeability: III. The Effect of Lack of Oxygen on Permeability, Am. J. Physiol. **83**:528, 1928. Bayliss (footnote 30).

32. Bayliss (footnote 30).

33. Hirschfelder, A. D.: Antagonization of the Narcotic Action of Magnesium Salts by Potassium Sodium and Other Monovalent Cations, with a Contribution to the Theory of Narcosis and Analgesia, J. Pharmacol. & Exper. Therap. **37**:399, 1929. Bayliss (footnote 30). Leathes (footnote 28).

which may behave erratically in epilepsy. This possibility is suggested by the facts, first, that section or stimulation of a nerve going to an organ changes the permeability of its cells and secondly, that the functions of certain of the known hormones apparently involve cell membrane permeability.

SUMMARY AND CONCLUSIONS

1. Intensive studies of the water and mineral balances have been made in the case of a severely epileptic girl under experimental conditions in which changes in the state of hydration of the body have been induced by various procedures, other than water restriction.

2. The establishment of a positive water balance was regularly followed by convulsive seizures, excepting one period when intensive phenobarbital therapy was used. Convulsions, which occurred during two of the periods with slightly negative total water balances, actually followed temporary storage of water.

3. Higher levels of water exchange do not necessarily favor the occurrence of convulsions if active diuresis or catharsis prevents water retention.

4. During periods of diuresis when no seizures occurred, sodium and chlorine were the predominating minerals of the urine; whereas, during the alternating periods of rehydration, when seizures occurred, potassium showed a negative balance with a striking increase in the potassium to sodium ratio.

5. During periods of positive water balance the increase in the potassium to sodium ratio actually manifested itself from twelve to thirty-six hours before seizures occurred.

6. This apparent "leakage" of potassium from the cells, which was most marked during a period of sustained pituitary antidiuresis, may indicate an innate weakness in the retaining membranes, presumably of the cells of the central nervous system. It is possible that abnormal amounts of water and even sodium found entry to the cells at the same time.

7. The data recorded are tentatively interpreted as favoring the view that an inherent defect in the mechanism for regulating permeability of the brain cell membranes is characteristic of the epileptic state.

8. The specific action of phenobarbital would appear from the limited data presented to be that of maintaining the normal relationships of the electrolytes and water on the two sides of the cell membrane.

THE RESPIRATORY METABOLISM IN INFANCY AND IN CHILDHOOD

XIV. THE EFFECT OF THYROID THERAPY ON THE METABOLISM OF PROTEIN IN NORMAL INFANTS

L. E. WEYMULLER, M.D.
BROOKLYN
T. C. WYATT, M.D.
SYRACUSE, N. Y.
AND
S. Z. LEVINE, M.D.
NEW YORK

WITH THE TECHNICAL ASSISTANCE OF M. KELLY, R.N.

The calorigenic action of thyroid extracts in normal infants was demonstrated in the preceding paper of this series.[1] The increased expenditure of energy was shown to be due to an accelerated combustion of fat and of carbohydrate in proportions similar to those metabolized under basal conditions, as indicated by the constant levels of the respiratory quotients before and during treatment with the extracts. These results corroborate in part studies of adults [2] showing that under the stimulus of an excess of thyroxine the body cells consume at an accelerated rate whatever type of food is brought them.

The preceding study, however, gave no information regarding the metabolism of protein, since the nitrogen elimination in the urine was not determined during calorimetric observations. This supplementary study of protein metabolism was therefore undertaken to make available complete data for determining the character of the intermediary metabolism of the essential foodstuffs in the normal, growing organism during thyroid medication.

At one time, a "toxic destruction" of protein was considered to be as characteristic a function of the thyroid hormone as its calorigenic

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From the Department of Pediatrics, Cornell University Medical College, and the New York Nursery and Child's Hospital.

1. Wyatt, T. C.; Weymuller, L. E., and Levine, S. Z.: The Respiratory Metabolism in Infancy and in Childhood: XIII. The Calorigenic Action of Thyroid Extracts in Normal Infants, Am. J. Dis. Child. **43**:845 (April) 1932.

2. Boothby, W. M., and Sandiford, I.: The Total and the Nitrogenous Metabolism in Exophthalmic Goiter, J. A. M. A. **81**:795 (Sept. 8) 1923.

action.[3] More recent investigations, however, on adult patients with hyperthyroidism and on normal men following the administration of thyroid extracts do not support this earlier view.[4] The evidence at present available seems to indicate that an excess of thyroxine in the tissues of the fully grown organism, whether the excess is spontaneous or induced, causes no demonstrable change in the true endogenous protein metabolism.[5] No similar studies for infants are available in the literature. This gap in present knowledge and the conflicting evidence recorded in the early and in the more recent studies of adults suggested the investigation of normal infants.

METHODS OF STUDY

Subjects.—The five male infants previously studied comprised the present series. They were from 4 to 17 months old, were in various states of nutrition, and possessed presumably normal thyroid glands as revealed by their basal metabolic rates. They were afebrile and free from acute infections and alimentary disturbances during the periods of study. A summary of their nutritional status was given in table 1 of the previous paper.[1]

Diets.—With few exceptions (table 1 of this paper), the infants received meals of uniform composition and a constant fluid intake throughout the periods of observation of from one to three months. The diets either consisted entirely of whole milk dilutions or were supplemented with cereals and green vegetables in the older infants. The daily caloric and protein intake as estimated from standard tables[6] ranged between 93 and 149 calories and between 4.3 and 6.4 Gm. per kilogram of body weight, respectively, for the different subjects. These diets, which were ingested without losses by all except one infant (J. S.),

3. Magnus-Levy, A.: Metabolism in Diseases of the Ductless Glands, in von Noorden: Metabolism and Practical Medicine, Chicago, Keener & Company, 1907, vol. 3, p. 983.

4. Du Bois, E. F.: Metabolism in Exophthalmic Goiter, Arch. Int. Med. **17**: 915 (June) 1916. Müller, F.: Zur Therapie der Schilddrüse, Therap. d. Gegenw. **66**:49 and 97, 1925. Deuel, H. J., Jr.; Sandiford, I.; Sandiford, K., and Boothby, W. M.: The Effect of Thyroxin on the Respiratory and Nitrogen Metabolism of a Normal Subject Following Prolonged Nitrogen-Free Diet, J. Biol. Chem. **76**:407 (Feb.) 1928.

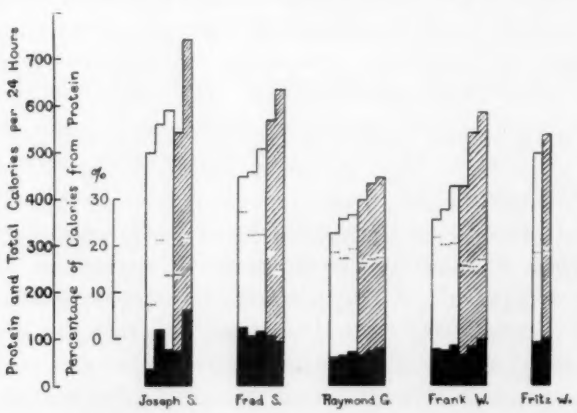
5. Boothby, W. M.; Sandiford, I.; Sandiford, K., and Slosse, J.: The Effect of Thyroxin on the Respiratory and Nitrogenous Metabolism of Normal and Myxedematous Subjects: I. A Method of Studying the Reserve or Deposit Protein with a Preliminary Report of the Results Obtained, Tr. A. Am. Physicians **40**:195, 1925.

6. Rose, M. S.: Laboratory Handbook of Dietetics, ed. 2, New York, The Macmillan Company, 1923.

were apparently adequate for maintenance but not for proper growth as judged by the stationary weight curves.

Energy Metabolism.—The heat production of each infant was measured in a respiration chamber of the Benedict-Talbot type [7] at regular intervals preceding and during treatment with the different thyroid preparations. The calorimetric data and metabolic results were reported in detail in the last paper. For purposes of reference, some of the essential data are again presented in table 1 of this paper.

Urine.—Collections of the urine were begun on the mornings following calorimetric observations and continued for twenty-four hours.[8] In all, twenty-five such specimens were obtained without losses in the five infants, thirteen under basal conditions and twelve during medication



The daily energy metabolism and the calories derived from the combustion of protein preceding (blank columns) and during (shaded columns) thyroid administration. The entire columns represent the total daily calories; the black areas, the protein calories. The dash lines indicate the percentage of total calories derived from protein.

with the thyroid extracts. The specimens were analyzed in duplicate or triplicate for total nitrogen by the macromethod of Kjeldahl after preliminary examination had established the absence of preformed protein. The grams and calories derived from the metabolism of protein were obtained by multiplying the grams of urinary nitrogen by 6.25 and

7. Benedict, F. G., and Tompkins, E. H.: Respiratory Exchange, with a Description of a Respiration Apparatus for Clinical Use, Boston M. & S. J. **174:** 857 (June 15), 898 (June 22) and 939 (June 29) 1916.

8. Hoag, L. A.: Apparatus for the Quantitative Collection of Urine and Stools of Male Infants, Am. J. Dis. Child., to be published.

26.51, respectively. This procedure afforded an index of the protein metabolized by the infants at the changed levels of total metabolism induced by thyroid therapy. This method of comparing the total metabolism obtained under basal conditions with the protein metabolized under daily maintenance conditions is admittedly not ideal. It was, however, preferred for our purposes, as analyses of the total nitrogen elimination in twenty-four hours obviate such interfering factors as "nitrogen lag," and undoubtedly afford a better index of the true protein metabolism than do calorimetric specimens of several hours' duration. Moreover, it has been shown [9] that slight activity in adults paralleling that of our infants during the periods of collection exerts only a trivial influence on the intermediary metabolism of protein. Finally, the employment of the same procedure during control periods and during periods of treatment establishes the reliability of the results for purposes of comparison.

It is obvious that this study is concerned solely with the total protein metabolism and makes no attempt to differentiate the endogenous protein metabolism from that derived from exogenous sources (deposit or reserve protein), since the nitrogen partition products in the urine were not separately estimated.

Nitrogen Balance.—The nitrogen excretion in the feces was not determined. This fraction was estimated to comprise 10 per cent of the nitrogen intake, as is the usual custom in calculating the nitrogen balance. The stools of all of the subjects were normal in number and consistency throughout the periods of study. Nitrogen balances are available for only four infants because of refusal and vomiting in one subject (J. S.)

Thyroid Therapy.—Thyroid preparations of varying potency [10] were employed to elevate the metabolism to different levels. The nitrogen elimination was determined, and the protein metabolism was estimated only after the metabolic rate had attained its maximum level with each type of drug. This method of approach is adequate for a comparison of the protein with the total energy metabolism only at well sustained metabolic levels. It does not furnish data of the protein metabolism during periods of transition from lower to higher metabolic levels or vice versa.

9. Lusk, G.: The Elements of the Science of Nutrition, ed. 4, Philadelphia, W. B. Saunders Company, 1928, p. 402.

10. The thyroid preparations included the whole gland product (Burroughs-Wellcome), the desiccated extract (Armour) and synthetic thyroxine (Hoffmann-LaRoche).

TABLE 1.—*Thyroid Dosage and Dietary, Urinary and Calorimetric Data per Twenty-Four Hours*

		Diet		Urine		Nitrogen	Metabolism			Calories from	Basal Metabolic Rate,§	Thyroid		
								Calories†			Deviation			
	Date	Calories	Nitrogen, Gm.	Volume, Cc.	Nitrogen, Gm.	Balance,# Gm.	Respiratory Quotient	Protein‡	Total	Protein, per Cent	from Standards, per Cent	Dose	"Type"	Days
Joseph S.....	11/10/30	1,263*	7.00	85	1.39	.....	0.852	36.8	498	7.4	— 1	.....	Basal	
	12/ 3/30	1,263	7.00	246	2.79	.....	0.844	74.0	541	13.6	+ 6	12 grains (0.78 Gm.)	Whole	5
	12/ 5/30	1,263	7.00	192	3.66	.....	.....	97.0	...	....	....	12 grains (0.78 Gm.)	Whole	7
	2/18/31	1,263	7.00	166	2.97	.....	0.835	78.7	589	13.4	+ 7	.....	Basal	
	3/14/31	1,263	7.00	411	6.06	.....	0.879	160.7	742	21.7	+32	15 grains (0.97 Gm.)	Desiccated	8
	3/27/31	1,263	7.00	261	4.46	.....	0.866	118.2	561	21.1	— 4	0	.....	11
Fred S.....	12/ 9/30	852	5.76	811	4.56	+0.6	0.879	120.9	446	27.1	+ 9	.....	Basal	
	12/23/30	852	5.76	756	3.91	+1.3	0.820	103.7	569	18.2	+40	10 grains (0.65 Gm.)	Desiccated	8
	12/31/30	852	5.76	893	3.85	+1.3	0.894	102.1	457	22.3	+10	0	.....	7
	1/16/31	852	5.76	498	3.53	+1.7	0.876	93.6	633	14.8	+52	10 grains (0.65 Gm.)	Desiccated	10
	1/29/31	984	5.92	928	4.29	+1.0	0.846	113.7	507	22.4	+13	0	.....	11
Raymond G.....	2/ 4/31	452	3.80	465	2.29	+1.1	0.880	60.7	327	18.6	+ 7	.....	Basal	
	2/16/31	452	3.80	403	2.43	+1.0	0.833	64.4	398	16.2	+24	10 grains (0.65 Gm.)	Whole	8
	2/23/31	452	3.80	409	2.65	+0.8	0.889	70.3	364	19.3	+14	0	.....	6
	3/ 7/31	452	3.80	360	2.77	+0.7	0.885	73.4	431	17.0	+36	10 grains (0.65 Gm.)	Desiccated	8
	3/28/31	524	4.30	408	2.92	+1.0	.....¶	77.4	445	17.4	+38	1 mg.	Thyroxine	8
	4/18/31	656	4.80	207	2.30	+2.0	0.842	61.0	357	17.1	+10	0	.....	23
Frank W.....	2/ 7/31	585	3.96	896	2.89	+0.7	0.870	76.6	353	21.7	+30	.....	Basal	
	2/17/31	669	4.44	626	2.49	+1.5	0.875	66.0	422	15.6	+47	10 grains (0.65 Gm.)	Whole	8
	2/28/31	669	4.44	850	2.83	+1.2	0.930	75.0	376	20.0	+25	0	.....	10
	3/ 9/31	669	4.44	296	3.12	+0.9	0.882	82.7	541	15.3	+80	10 grains (0.65 Gm.)	Desiccated	8
	3/27/31	669	4.44	477	3.72	+0.3	0.850	98.6	584	16.9	+83	1 mg.	Thyroxine	6
	4/17/31	669	4.44	325	3.24	+0.8	0.909	85.9	423	20.3	+24	0	.....	22
Fritz W.....	3/ 4/31	792	5.00	559	3.40	+1.1	0.838	90.1	494	18.2	+24	.....	Basal	
	3/17/31	792	5.00	264	3.75	+0.8	0.880	99.4	537	18.5	+34	10 grains (0.65 Gm.)	Desiccated	11

* The nitrogen excretion in the feces is assumed to be 10 per cent of the nitrogen intake in computing the nitrogen balance.

† The nitrogen in the urine was not determined. The heat production was calculated on the assumption that 15 per cent of the calories were derived from the combustion of protein.

‡ The protein calories were obtained by multiplying the urinary nitrogen (in grams) by 26.51.

§ The standards for basal metabolism were estimated from the body weight and body stature.

The nitrogen balance was not obtainable because of the refusal and vomiting of food.

‖ No measurement of the energy metabolism was made on this day.

¶ There was a leak in the oxygen cylinder. The heat production was calculated from the carbon dioxide at an assumed respiratory quotient of 0.885.

RESULTS

The essential data relating to the diets, urine and energy metabolism of the infants are presented in table 1. Table 2 and the accompanying chart are arranged to show the relation between the protein and the total metabolism at the varying metabolic levels preceding and during thyroid therapy.

A study of the protein metabolism, embracing the nitrogen elimination in the urine, the grams of protein metabolized, the calories derived from the combustion of protein and the nitrogen balances, is

TABLE 2.—*Relation of Basal Metabolic Rate to Protein Metabolism Preceding and During Thyroid Therapy*

	Basal Metabolic Rate; Deviation from Standards, per Cent		Nitrogen Elimination in Urine, Gm.		Calories Derived from Combustion of Protein, per Cent		Nitrogen Balance, Gm.	
	Basal	Treated	Basal	Treated	Basal	Treated	Basal	Treated
Joseph S.	— 4	+ 6	4.46	2.79	21.1	13.6	.....	.....
	— 1	*	1.39	3.66	7.4	....	.....	.....
	+ 7	+32	2.97	6.06	13.4	21.7	.....	.....
Fred S.	+ 9	+40	4.56	3.91	27.1	18.2	+0.6	+1.3
	+10	+52	3.85	3.53	22.3	14.8	+1.3	+1.7
	+13	....	4.29	....	22.4	....	+1.0	.....
Raymond G.	+ 7	+24	2.29	2.43	18.6	16.2	+1.1	+1.0
	+10	+36	2.30	2.77	17.1	17.0	+2.0	+0.7
	+13	+38	2.65	2.92	19.3	17.4	+0.8	+1.0
Frank W.	+24	+47	3.24	2.49	20.3	15.6	+0.8	+1.5
	+25	+80	2.83	3.12	20.0	15.3	+1.2	+0.9
	+30	+83	2.89	3.72	21.7	16.9	+0.7	+0.3
Fritz W.	+24	+34	3.40	3.75	18.2	18.5	+1.1	+0.8
Average	+12.8 ± 1.92	+42.9 ± 4.58	3.16 ± 0.178	3.43 ± 0.190	18.95 ± 0.882	17.01 ± 0.417	+1.06 ± 0.101	+1.02 ± 0.121
Difference Averages / Difference Probable Errors	30.1 ± 4.966		0.27 ± 0.259		1.94 ± 0.976		0.04 ± 0.157	

* The energy metabolism was not determined on this day.

so closely related in its various phases that the results may conveniently be considered under one heading. As previously mentioned, estimation of these components at various but well sustained levels of the energy metabolism served as a means of comparing the effect of the thyroid hormone on the protein and on the total energy metabolism in the normal infant. Widely dissimilar effects on the two mechanisms should be demonstrable to establish a specific toxin action of the autacoid on the protein metabolism. The evidence presented in table 2 and in the chart does not support this conception.

The following calculation of the average values in terms of absolute amounts and in terms of percentages prior to and during thyroid administration is of interest. The average increase in the daily heat production of the five infants of 89 calories (from 442.5 to 531.2) during thyroid therapy was accompanied by an absolute increase of only

0.27 Gm. (from 3.16 to 3.43 Gm.) in the urinary output of nitrogen and by a calculated increase of 7.2 (from 83.8 to 90.9) in the calories derived from the combustion of protein. The latter increases are slight and in accord with expectation. They are undoubtedly ascribable to the stimulation of the general metabolism and possibly also to a continued mobilization of exogenous protein reserves from the body. Boothby and his collaborators [11] found that the nitrogen elimination in the urine of two normal adult subjects required ten and twelve days following single intravenous injections of thyroxine to return to the original basal levels. The average nitrogen balances remained essentially unchanged (from + 1.06 to + 1.02 Gm.). The results, expressed as percentages, are of greater significance and serve to correlate the various increments of increase with each other. With an average rise in the metabolic rate of the five infants of 30 per cent (from + 13 to + 43), the percentage of calories derived from the combustion of protein fell 1.9 (from 18.95 to 17.01). The fraction contributed by protein to the total heat production was, therefore, actually less at the high metabolic levels with thyroid administration than at the lower levels in the control periods. The differences are comparatively slight.

The minor differences in the average figures for urinary nitrogen, protein calories and nitrogen balances, as well as the marked variations present in individual infants before and during thyroid medication, made it imperative to subject the results to statistical analysis in order to evaluate the significance of the deviations. The results of this analysis (table 2, last line) indicate that the differences are statistically insignificant and presumably the result of random sampling.[12]

The results seem adequate to establish that the stimulation of the energy metabolism in the normal infant by thyroid therapy is not necessarily at the expense of an excessive combustion of protein. In other words, a "toxic destruction" of protein is apparently not a necessary or a usual accompaniment of the calorigenic action of the thyroid hormone in normal infants. These results are in accord with the recent studies on adults by Boothby and his associates.[5] They found that after equilibrium had been established at high metabolic levels in response to thyroid administration, the protein metabolism as estimated from the nitrogen elimination in the urine declined from the transitory elevated to the original basal level. Whether deposit protein is mobilized

11. Boothby (footnotes 2 and 5).

12. The differences between the means before and during treatment with the thyroid products were in no instances significantly greater than the differences between their respective probable errors. It may be noted that the differences in the percentages of calories derived from the oxidation of protein before and during treatment are on the borderline of significance (the differences between the means being approximately twice the differences of the probable errors).

from the body of infants with a consequent partial depletion of the exogenous protein reserves during the periods of transition from lower to higher metabolic levels, as the foregoing authors found in adults, is not ascertainable from this study. The evidence is, however, adequate to show that the true endogenous protein metabolism of normal infants is not significantly accelerated as the result of thyroid medication.

CONCLUSIONS

A combined study was made of the respiratory metabolism and of the nitrogen elimination in the urine of normal infants preceding, during and following the administration of thyroid extracts.

The results show that the calorigenic action of the hormone in these subjects is ascribable to an accelerated combustion of all three foodstuffs—protein, carbohydrate and fat. No evidence was found of a "toxic destruction" or of an excessive combustion of protein. The latter is, therefore, not a usual or a necessary accompaniment of the calorigenic action of the thyroid hormone in normal infants.

161 West Sixty-First Street, New York.

Progress in Pediatrics

GANGLIONEUROMA

REPORT OF TWO CASES WITH A REVIEW OF THE LITERATURE

JOHN A. BIGLER, M.D.
AND
ARCHIBALD HOYNE, M.D.
CHICAGO

Ganglioneuromas have been reported with rarity in children. Because of this fact and on account of the difficulties encountered in diagnosis, we are describing two recently observed cases.

These tumors of the sympathetic nervous system may give rise to symptoms, over a long or a short period, by pressure on or displacement of adjacent organs or tissues. Our first case is a vivid example of this. The tumor occurred in the mediastinum, causing compression and displacement of the trachea with the signs and symptoms of laryngeal or tracheal obstruction. When the patient was first seen by us, the diagnoses of laryngeal diphtheria, a foreign body in the air passages, polypi of the larynx, acute tracheitis, retropharyngeal abscess, hyperplasia of the peritracheal or peribronchial lymph nodes, hypertrophy of the thymus, mediastinal abscess and mediastinal tumor were considered. Many of these conditions were immediately eliminated. Roentgen examination of the chest showed a wide mediastinal shadow, which was interpreted as being due to some form of new growth rather than to hyperplastic lymph nodes (fig. 1).

If we had known then what we have learned since about these tumors, it is possible that the nature of the mass might have been suspected and the only hopeful treatment, operative removal, instituted. Ten ganglioneuromas occurring in the mediastinum have been reported in the literature, five of which were in children. Five of these ten patients, including four of the children, were operated on, with three complete recoveries and two deaths. It is interesting to note that although the first case was reported in 1870, five of the ten cases have been reported since 1923. It is only in the last five that surgical treatment was used, with the results just cited.

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From the Children's Memorial Hospital and the Otho S. A. Sprague Memorial Institute Laboratory.

However, when ganglioneuromas are present, they usually develop in locations where no symptoms are produced, and under such circumstances the tumor is often a chance observation at necropsy. Our second case is an illustration of this.

We have reviewed the literature and have attempted to collect and classify all the reported cases of ganglioneuroma.

REPORT OF CASES

CASE 1.—*History.*—T. A. (referred by Dr. A. Weigan), a white boy, 5 years of age, entered the Children's Memorial Hospital on Feb. 22, 1929, at 1:30 a. m.,

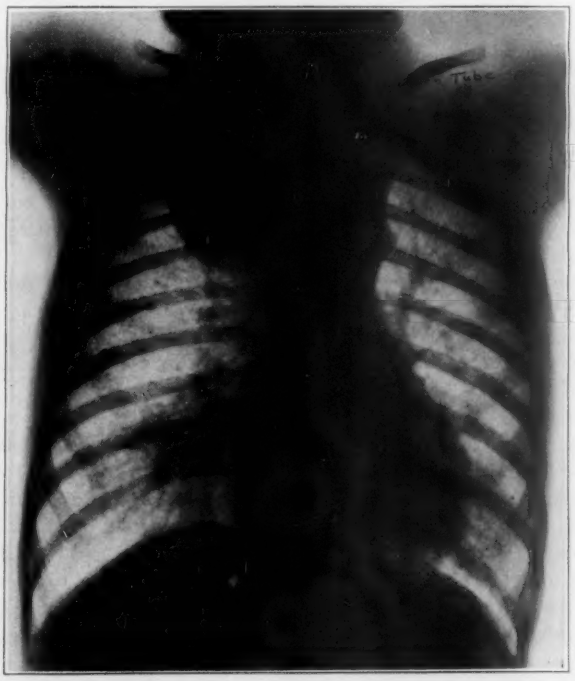


Fig. 1.—Mediastinal tumor mass with displacement of the trachea as shown by the shadow of the intubation tube.

with the following history: He had acquired a cold accompanied by cough six days previously. However, he was up and playing about the house until two and one-half hours before admission, when he suddenly became cyanotic and dyspneic. Morphine, atropine and epinephrine were administered at home by a physician. These drugs gave some relief, but the cyanosis and dyspnea recurred, and on arrival at the hospital the boy was semicomatose and deeply cyanotic.

Since the age of 2 years the patient had had some difficulty in breathing on exertion and excitement. When quiet he seemed to breathe normally. The family physician had treated him for asthmatic attacks since the age of 2 years. These attacks were characterized by cyanosis and noisy and difficult breathing. The

seizures had not been worse at night. In November, 1928, the patient experienced a severe dyspneic attack which was diagnosed as diphtheria, and 30,000 units of diphtheria antitoxin was administered. The dyspnea recurred on the sixth day, and 20,000 units more was administered.

The history revealed that the child had had pertussis at the age of 2 years, and had had measles, chickenpox, mumps and diphtheria (?) since then. The family history was unimportant.

Examination.—Examination revealed a well nourished, well developed, acutely ill child. There were cyanosis and dyspnea and also unconsciousness. Deep substernal retraction, but no suprasternal retraction, was present. The pupils were the size of a pinpoint. There was no edema or redness of the throat and no membrane was seen in the pharynx, but there was a suggestion of an obstruction in the larynx or trachea.

Course.—Immediately on the admission of the patient to the hospital, laryngeal intubation was performed with a 5 to 6 year tube. As there was no relief, the tube was removed, and the boy was placed in a croup tent. The temperature was 105 F. by rectum; the pulse rate, 200; respirations were 44 per minute. Oxygen was administered and the patient's color improved. At 2 a. m., he became more cyanotic and seemed to be expiring. Intubation was again performed with a 6 to 7 year tube, which afforded almost instant improvement in his condition. He regained consciousness and was able to drink water. The temperature decreased to 101.6 F. rectally, the pulse rate to 148, and the respiratory rate to 40. At the time of the second intubation, it was noted that the tube did not follow the median line, but deviated sharply to the left. This led to the conclusion that the trachea was pulled or pushed to one side and that the cause of the cyanosis was external to the larynx or trachea. Roentgen examination disclosed a tumor of the upper right part of the mediastinum, which will be fully described later.

Examination of the blood showed: red blood cells, 3,248,000 per cubic millimeter; white blood cells, 20,200; hemoglobin, 75 per cent; polymorphonuclear neutrophils, 82 per cent; large lymphocytes, 11 per cent, and small lymphocytes, 7 per cent. Aside from a 4 plus albumin reaction, the urine was normal. Cultures from the nose and throat were negative for the Klebs-Loeffler bacillus.

On the patient's second day in the hospital, restlessness and cyanosis developed again; the 6 to 7 year intubation tube was removed, and an 8 to 9 year tube was inserted. This seemed to alleviate the difficulty in breathing to a considerable extent. However, on February 25, the restlessness was again evident; a special, long (8.75 cm.) intubation tube was introduced, but failed to accomplish the results desired. This tube was used in the belief that it might be possible to efface the sharp bend in the trachea. Had our purpose fully succeeded, we hoped to give roentgen therapy, which had already been started, in an endeavor to reduce the size of the tumor. Unfortunately, the long tube was not a success, and the shorter tube had to be reinserted. Bronchopneumonia developed, and the child died at 5 p. m. on February 27, five days after his admission to the hospital.

Autopsy.—Postmortem examination was made by Dr. W. G. Hibbs and one of us (Dr. Bigler). The anatomic diagnosis was: ganglioneuroma (mediastinal); marked compression and displacement of the trachea to the left; an intubation tube in the trachea; multiple mycotic abscesses of the lungs; diffuse bilateral bronchopneumonia; hyperplasia of the cervical, mediastinal and peribronchial lymph nodes; emaciation; clot-distended right chambers of the heart; retraction of the body of the sternum; dry and crusted lips; petechial hemorrhages into the lining of the stomach; cloudy swelling of the myocardium, liver, kidneys and pancreas; passive

hyperemia of the liver, kidneys and intestines; moderate fatty changes of the liver and cortex of the kidneys; paralytic ileus; atrophy of the thymus; hyperplasia of the lymphoid tissue of the lining of the intestines; two small accessory spleens, and a circumcised penis.

In the right portion of the mediastinum, opposite the first two thoracic vertebrae, there was a mass protruding 6 cm. to the right of the spinal column and extending 6 cm. parallel to it. This mass compressed the apex of the right lung above; medially it compressed the trachea and displaced it to the left. The tumor was hard, oval and covered with pleura. It was encapsulated and lobulated, one lobule making up at least two thirds of the entire mass. This tumor weighed 110 Gm. and measured 7 by 6.8 by 2.5 cm. (fig. 2). The surfaces made by cutting were generally smooth and sprinkled with pinpoint-sized orange-yellow areas, and in the periphery there was a distinctly streaked, friable, red-brown tissue.

Under the right clavicle there was a similar mass, which measured 4 by 3 by 1.3 cm. It was firm and flat, and when cut across resembled the larger tumor in all essentials. No connection with a nerve or ganglion was found in either instance.

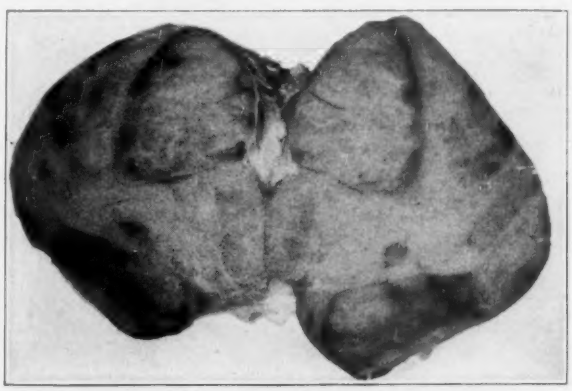


Fig. 2.—The gross appearance of the tumor when sectioned.

The cervical lymph nodes of the right side of the neck were prominent and averaged about 1 cm. in diameter. They were smooth and gray when cut across. The peribronchial lymph nodes were all increased in size, so that in general they measured from 1 to 3 cm. in diameter. They were red, and when cut across had a smooth, homogeneous red to gray surface.

Microscopic examination was made in the Neurological Laboratory of the University of Chicago, by Dr. S. S. Allen. The following staining methods were used on paraffin sections: hematoxylin and eosin, phosphotungstic acid hematoxylin, Loyez stain for myelin sheaths, toluidine blue and cresyl violet. By the following methods preparations were made from frozen sections: Perdrau's method for connective tissue; Cajal's pyridine silver method; Hortega's silver carbonate method; the Bielschowsky method for nerve fibers; Hortega's first and fourth variants of Achucarro's method; Cajal's gold sublimate method; Penfield's method, and Herxheimer's scarlet red method for fat.

The tumor was composed of two definite types of tissue, neurinomatous and nerve (fig. 3). The former consisted of fusiform cells more or less compactly arranged. The nuclei were small, elongated or oval, and deeply stained; they

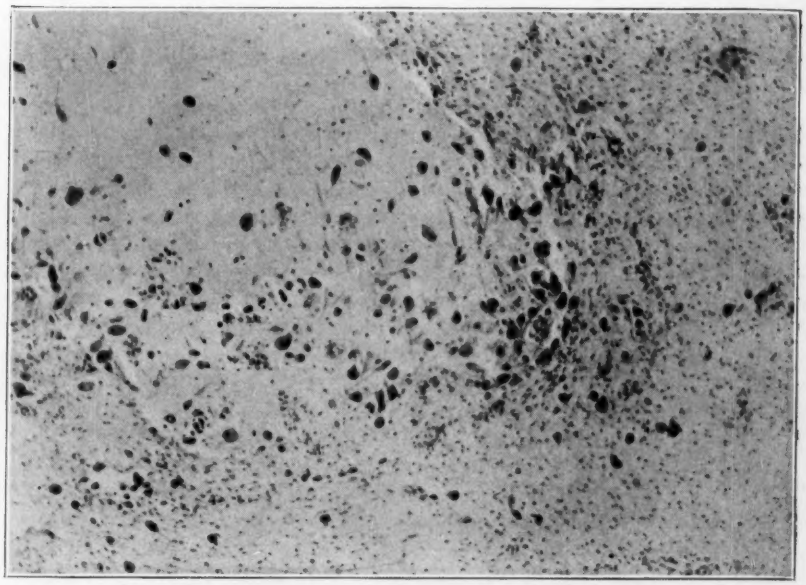


Fig. 3.—Photomicrograph of the tumor. Note the island of nerve tissue containing most of the ganglion cells, surrounded below and to the right by neurinomatous tissue. Hematoxylin and eosin; × 75.

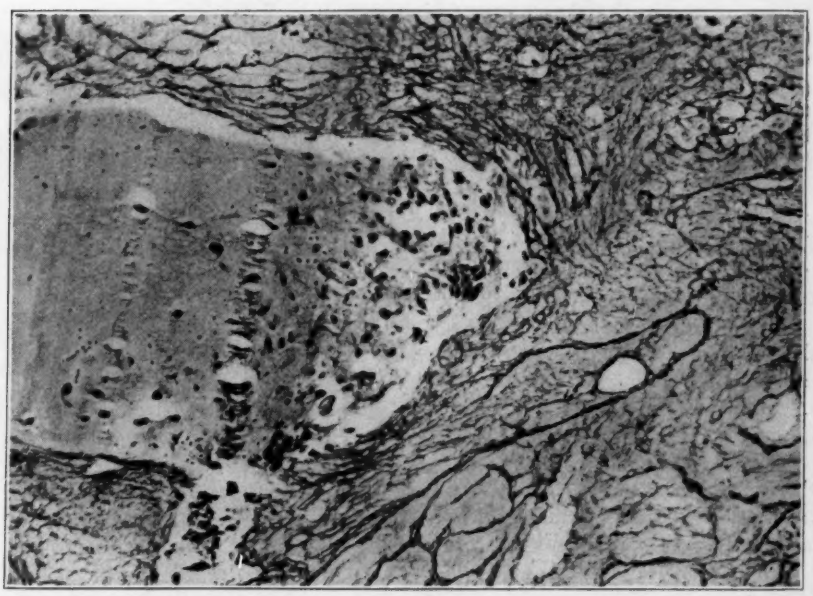


Fig. 4.—Note the absence of reticulin in the island of nerve tissue and the abundance of reticulin in the neurinomatous area. Perdrau's method; × 75.

contained small particles of chromatin. No mitotic figures were found. Fine wavy fibrils were seen interspersed among the cells. In some areas the cells were so arranged as to form bundles of various thicknesses. In other areas these bundles were shown in cross-section, which gave the tissue a lobulated appearance. The bundles stained pink in hematoxylin and eosin and pinkish-red in the phosphotungstic acid hematoxylin preparations. Perdrau's method showed them to be composed of fine wavy fibrils or reticulum (fig. 4), the fibrils being somewhat coarser toward the periphery of the bundles. Boundaries of small, thin-walled vessels could be seen in the bundles, both in longitudinal and cross-section. Cajal's pyridine silver method showed fine, delicate, blackly impregnated fibers in the coarse bundles of yellowish-brown reticulum. There were small varicosities at various intervals along their course. These black fibrils were not abundant and might be entirely lacking in various parts of the tissue. They could also be seen

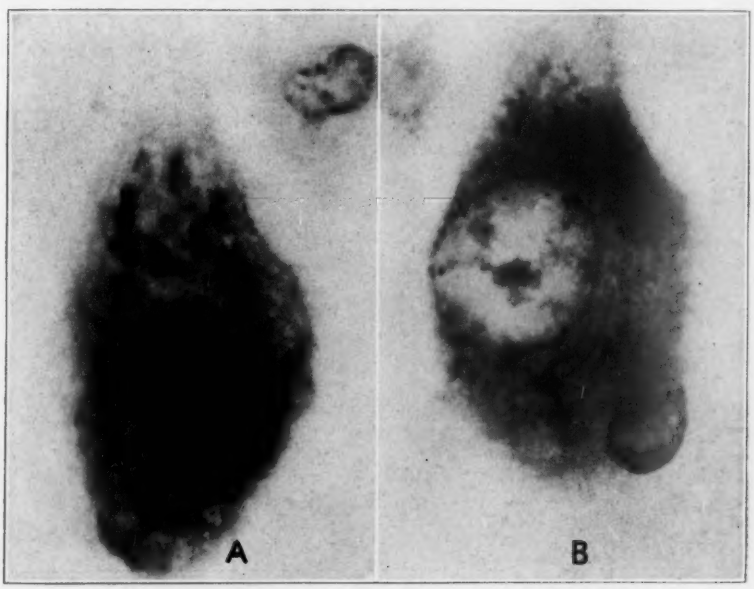


Fig. 5.—Neoplastic ganglion cells with tigroid bodies. Toluidine blue; × 2,000.

in the Bielschowsky preparations, but there was not such a striking contrast between the fibers and the background. No myelin sheaths could be demonstrated.

Scattered throughout these bundles of connective tissue were seen large, globular, flask-shaped and multipolar cells, occurring singly and in definite islands standing out in contrast to the surrounding tissue. The cytoplasm was finely granular, and was pinkly stained in the hematoxylin and eosin preparations. The majority of these cells, especially the larger ones, had one, two and sometimes three processes extending out from the cell body. These processes were well brought out by the silver carbonate method of Hortega and could be seen to extend various distances from the cell body proper. Several cells were observed to be joined by a single process. The cresyl violet and toluidine blue sections showed deeply stained flakes of tigroid substance in the cytoplasm near the periphery in many of the larger, better developed cells (fig. 5). The nuclei of these cells were large and round, some staining more deeply than others and having

a coarsely granular appearance. Some of the cells contained two nuclei. A nucleolus could be seen in many of the nuclei. In most of the cells the nucleus was eccentric. The great majority of these cells were large and well developed, resembling adult ganglion cells. Some, however, were small and misshapen, especially in closely packed clumps in the islands. Very few suggested degeneration, and no fat droplets were seen anywhere in the sections stained by Herxheimer's scarlet red.

Although the neurinomatous tissue was much more abundant than the nerve tissue, these islands of ganglion cells were quite numerous. They were fairly well defined, but there was no evidence of encapsulation of any of the individual cells. The intercellular substance in the islands appeared homogeneous in the hematoxylin and eosin sections, and Perdrau's method showed the islands to be entirely lacking

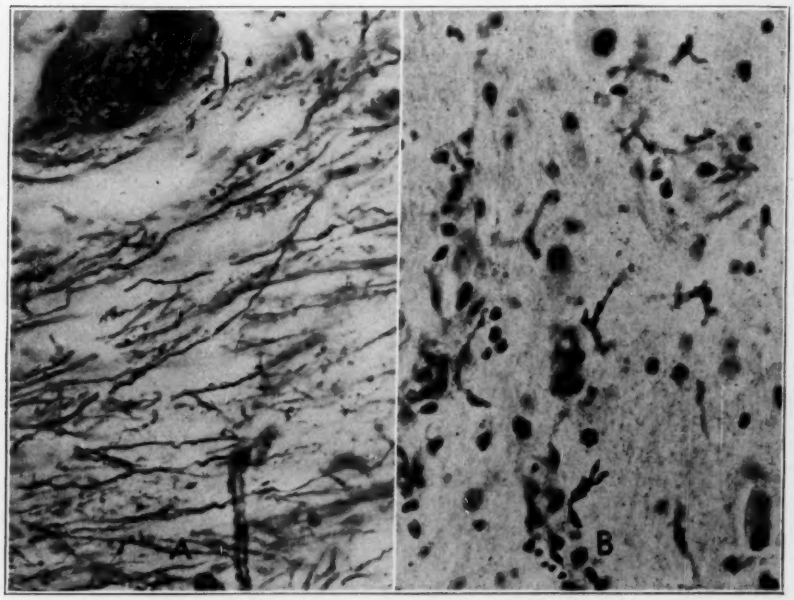


Fig. 6.—*A*, unmyelinated nerve fibers showing typical varicosities. Cajal's pyridine-silver; × 800. *B*, microglial cells near the ganglion cells. Globus-Penfield modification of Hortega's silver carbonate method; × 325.

in connective tissue. It was in these areas that nerve fibrils were seen to be most abundant, as shown by the methods of Cajal and Bielschowsky. The fibrils traversed the islands in all directions (fig. 6). Some were coarser than others, but no myelin sheaths were present. Many of the processes of the larger cells were seen to contain neurofibrils extending to the cell body (fig. 7). In most of the preparations interstitial cells in these ganglion cell islands appeared to be deficient. Penfield's method, however, showed numerous small branched cells, in which the nuclei were elongated, finely granular and deeply stained and the cytoplasm was homogeneous and extending out into minute processes. Fine, indistinct projections were observed extending out at right angles from many of the processes. These cells closely resembled microglia (fig. 7). Some of them were larger than others. The nuclei in the larger cells were more rounded and appeared

to be reticulated, and the processes were fewer. Several of the cells contained two nuclei. Other similar cells were almost entirely devoid of processes, the cell bodies ovoid and the nuclei vesicular. These cells might be interpreted as transitional types of microglia cells. Cajal's gold sublimate method failed to reveal any major glia cells in any part of the tissue.

CASE 2.—G. S., a Negro boy, 4½ years of age, entered the Children's Memorial Hospital with the diagnosis of celiac disease and idiocy. The history and clinical course of the illness can be omitted, because they have no bearing on the ganglioneuroma, which was a chance observation at necropsy.

Postmortem examination was made by Dr. W. G. Hibbs. The anatomic observations were: emaciation; generalized anemia; fatty changes of the liver and the lining of the aorta; hyperemia of the bowel and stomach; cloudy swelling

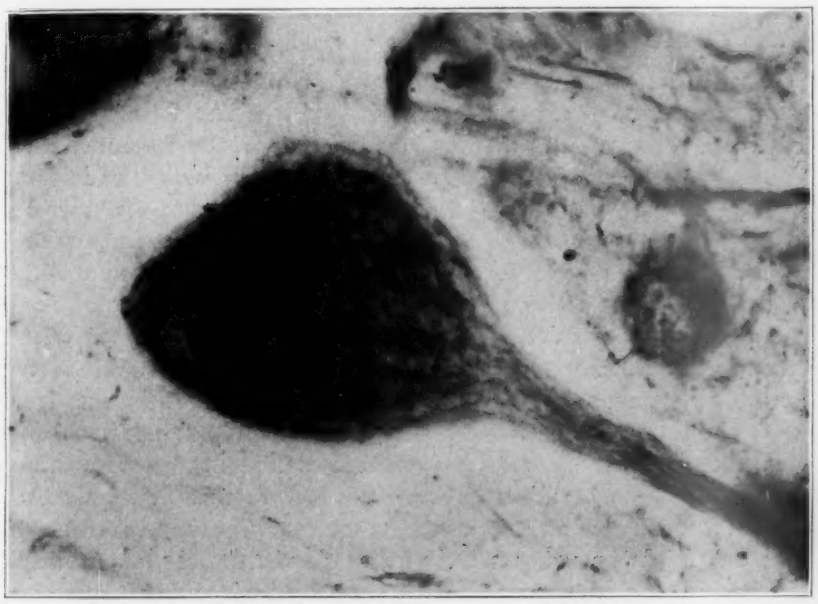


Fig. 7.—Neoplastic ganglion cell showing neurofibrils. Bielschowsky's method; × 1,400.

of the pancreas, liver and kidneys; ancient hemorrhage of the left lateral cerebral hemisphere; hypertrophy of the left ventricle of the heart; hypostatic edema and hyperemia of the lungs; hyperemia of the brain; edema of the leptomeninges; a foramen magnum pressure furrow at the base of the cerebrum, and retroperitoneal ganglioneuroma.

At the upper pole of the right kidney there was a tumor that measured 7 by 5.5 by 4 cm. It was removed with the right kidney in one mass and then sectioned in two equal parts. The tumor was distinctly encapsulated and definitely not a part of the kidney, to which it was attached by firm adhesions. The growth was generally smooth on the surfaces made by sectioning and was roughened only by delicate bands of firm tissue, giving a rather spongy appearance. There were small areas, generally from 3 to 5 mm. in diameter, that slightly mottled the surfaces and differed from the rest of the structure only in that they were a

little lighter gray than the adjacent tissue. There were no changes in the suprarenals, kidney pelves or ureters.

For microscopic examination sections were stained with hematoxylin and eosin. The tumor consisted of huge numbers of ganglion cells, compact in places, elsewhere only sparsely distributed, and indefinite bundles of nonmedullated nerve fibers coursing among the ganglion cells. There was a supporting structure of connective tissue and blood vessels. The ganglion cells were of the ordinary type.

HISTORICAL SKETCH

Nerve tissue is the most highly specialized tissue in the body. Tumors may arise from the central, the peripheral and the sympathetic nervous systems as well as from the suprarenals, the carotid gland, the coccygeal gland and Zuckerkandl's organ, which are a part of, or arise from, the nervous tissues.

The first use of the term "neuroma" was made by Odier in 1803. In 1863 Virchow classified nerve tumors as true and false neuromas. Loretz, in 1870, reported the first ganglioneuroma, stating that it arose from a prevertebral ganglion. In 1891, Marchand studied a tumor of the suprarenal gland and pointed out the similarity of its structure (neuroblasts) to that of the early embryonic sympathetic nervous system. Küster, in 1905, reported two cases of suprarenal tumors which he called gliomas, noting at the time a rosette arrangement of small lymphoid-like cells with fibrils in the center. In the same year Wiesel pointed out that these tumors of the suprarenals were not gliomas, but were tumors composed of embryonic sympathetic nerve elements from which the suprarenal medulla is formed. This was a decided step forward, but it was not until 1910 that the present conception of these tumors was brought about by Wright. Before that time, and even since then, many were reported as sarcomas, carcinomas, hypernephromas, lymphosarcomas, etc. It has only been through a comparative study that a true conception has been obtained of these neoplasms, individually, and of their relationship to each other in development.

HISTOGENESIS

A schematic diagram showing the development of the sympathetic nervous system prepared by Landau, as modified by Schultz, is given here.

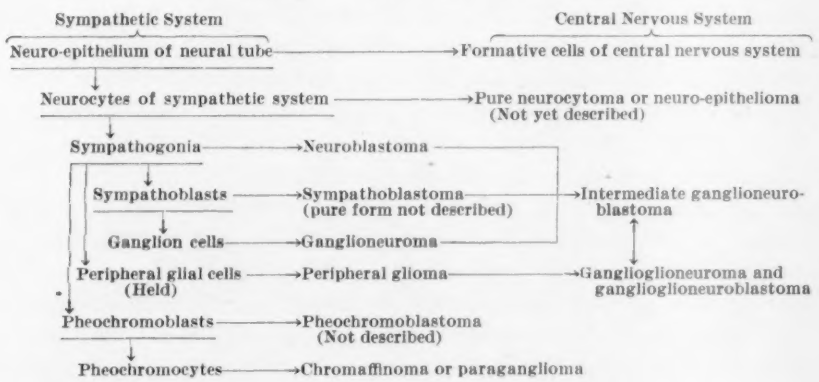
From the diagram it is seen that cells of the neurocanal go to make up both the sympathetic and the central nervous systems. The suprarenal medulla develops from the embryonic sympathogonia, while the carotid gland, the coccygeal gland and Zuckerkandl's organ, which are paraganglions, develop from the pheochromocytes.

The neurocyte is one of the earliest undifferentiated cells arising from the neurocanal. As yet no pure tumors composed only of these

cells have been described. The neurocytes by division form the sympathogonia, which are commonly called neuroblasts. The neuroblast is the potential cell from which all the tumors arise. It is a small cell about the size of a small lymphocyte for which it is frequently mistaken. The nuclei are hyperchromatic and resemble those of the small round cells of sarcomas. They may be grouped together to form rosettes, but this arrangement is not always present. The sympathogonia may give rise to two types of cells, the sympathoblast and the pheochromoblast. The sympathoblast is larger than its parent cell, but it is also a formative cell. It gives rise to the ripe ganglion cell with its axis-cylinders and fibrils which may be either medullated or nonmedullated.

Owing to this cell development, it can be seen how easily mixed types of tumors can develop, depending on the proliferation of the

Development of Sympathetic Nervous System



formative cells into ripe or unripe forms or both. There is no way of knowing from the location of the tumor or from its symptoms whether it is ripe and benign or unripe and malignant, unless metastasis has occurred. Nor is it possible to state when metastasis will take place in the forms that contain some undifferentiated cells.

Broadly speaking, three types of tumors may develop from the formative cells of the sympathetic system: neuroblastomas from neuroblasts, chromaffinomas or paragangliomas from the pheochromoblasts and ganglioneuromas from the adult ganglion cells. Intermediate or mixed types may occur. These tumors may be considered to be of congenital origin. It is commonly felt that they develop at the site of cell rests that have become misplaced or miscarried during the migration of the ganglionic crests during embryonic life. The cell rests may remain quiescent forever, or they may begin to proliferate at any period of antenatal or postnatal life. Although primarily tumors of the sympathetic system and its appendages, they may be found in the brain. As

both the brain and the sympathetic system develop from the neuroepithelium of the neurocanal, some of the formative cells may be misplaced during early development.

The neuroblastoma is the most common type found in children, and arises frequently in the suprarenals. It has been found in the mediastinum and elsewhere. It is a soft tumor which may be encapsulated, but which is usually invasive. It resembles a small cell sarcoma and may contain hemorrhages and areas of degeneration. Metastasis takes place early to the lymph nodes, the bones and the liver. Microscopically, the growth is composed of small lymphoid-like cells (sympathogonia or neuroblasts), which are distributed in a finely fibrillated matrix. The arrangement of the cells may be in rows, so that the characteristic rosette is seen with the ball of fibrils in the center. Rosette arrangement may be absent and the cells may be distributed along bundles of fibrils. Occasionally, the predominating cell may be the sympathoblast, but there are always many neuroblasts present. The sympathoblastoma is less common and less malignant than the neuroblastomas, and metastasis does not occur so readily.

The chromaffinoma is very rare. It is small and encapsulated, and seems to be benign. It may arise in the suprarenal medulla, the carotid gland, the coccygeal gland and Zuckerkandl's organ.

The ripe, true ganglioneuroma is rare in children. It is a firm, encapsulated, nodular, pale tumor, which varies in size from that of a pea to that of a man's head. It resembles grossly a fibromyoma. It may occur singly or in great numbers. Kredel and Beneke's patient had one hundred and sixty and Knaus' patient sixty tumors. Microscopically, it has a characteristic appearance which should not be confused with that of any other type of tumor. With the usual hematoxylin and eosin stain it is easily recognized, but for careful study special stains are necessary. Both nerve and neurinomatous tissues are present. Ganglion cells are seen singly and in groups in a dense tissue. They may be large, globular, flask-shaped, unipolar and multipolar. The cytoplasm is faintly granular and often contains tigroid substance. There are usually one or more processes extending out from the cell body. The nuclei are usually round, contain small granules, and are fairly deeply staining. Often a nucleolus is present. Frequently the cells are multinucleated, having sometimes as many as ten nuclei. Some of the cells may be small and misshapen as if they were degenerating. Naked axis-cylinders may be seen extending out from the ganglion cells. Neurofibrils are profuse and may be medullated or nonmedullated. There is often a disproportion between the number of neurofibrils and ganglion cells, which has led to much discussion. Some think that these nerve fibrils may develop from the sheath of Schwann cells, but the

most common and probable theory is that many of the ganglion cells disappear through degeneration. Cells resembling microglia were found in the tumor studied by us and have been found in a few others.

The largest part of the tumor consists of dense fibrous tissue which forms the framework and the septums of the lobulations. Areas of degeneration may be present. Calcifications have been found and often they have been of the ganglion cells.

The ganglioneuroma is considered benign when early formative cells are not present. Adult ganglion cells have been found in the adjacent lymph nodes in a few instances and have been described as metastatic. This is still a disputed point, however, as it is possible that these cells in the lymph nodes may represent individual tumors arising independently of the original tumor. In Berner's patient and in Beneke's second patient, however, evidence was very strong that the ganglion cells had metastasized. Peters, Freund, Wegelin, Fischer and others have described tumors that contained one or more groups of lymphoid-like cells. These cells have frequently been mistaken for lymphocytes but, when properly stained, they are found to be more granular and to have hyperchromatic nuclei. Evidence of proliferation may or may not be present. They are formative neuroblasts or sympathoblasts, and it is questionable whether the cells continue proliferating as unripe forms leading to malignancy and metastasis. In cases in which tumors containing such formative cells were removed surgically, there was no recurrence of the tumor or any metastasis. Histologically, in some of the tumors it seems quite certain that the formative cells develop into ripe ganglion cells. In others, there is no evidence that the proliferation is toward the development of ripe cells. It is in this last group that the question of malignancy is imminent, since in every case with true metastasis it is the formative cells that are found in the metastatic areas. Grossly, there is no way of establishing which tumors of this group may develop into malignant growths.

That typical ganglioneuromatous elements may occur in malignant metastasizing tumors is demonstrated in the cases of Dunn, Jacobsthal and Boyd. In Wahl's case ganglioneuromatous, neuroblastomatous and chromaffinomatous tissue were all present. Martius and Robertson each studied a case in which the main tumor was neuroblastomatous, with isolated small nodules and tumors that were typical ganglioneuromas. The case reported by Cushing and Wolbach is a unique one. At the age of 1 year the child had had a tumor removed from his back, which at that time was thought to be a sarcoma. The tumor recurred, and was removed ten years later, when it was found to be a typical benign ganglioneuroma. In reexamining the early sections, typical sympathoblasts were found, but no ganglion cells. Here, then, is a tumor that

during a period of ten years changed from a sympathoblastoma, which is considered malignant, to a benign ganglioneuroma. Why sympathoblasts at one period continue to produce the same undifferentiated cells while at another time they give rise to ganglion cells is unexplained.

In table 1 the simple ganglioneuromas are listed, and in table 2 tumors that are of the intermediate group. In some of the cases listed in table 1 complete microscopic observations were not reported. Four cases are included in group 2 in which ganglion cells were found in the adjacent lymph nodes. It is impossible to draw sharp lines between the simple and the intermediate types of tumors.

In the group of simple ganglioneuromas there are eighty-six cases, while in the intermediate group there are eleven cases, a total of ninety-seven. Of the eighty-six cases, the age of the patient is given in seventy-three; thirty-three (45.2 per cent) of the patients were children and forty (54.8 per cent) were adults, 16 years being considered the dividing age. Of the eleven patients in the intermediate group there were eight (72.7 per cent) children and three (27.3 per cent) adults, which is a rather striking difference. The more benign the tumor, the more advanced the age incidence. Neuroblastoma is found practically always in children. Taking the two groups together, there were forty-one children and forty-three adults. The youngest patient was a new-born infant, and the oldest was 73 years of age; both of these cases occurred in group 1.

In group 1 there are seventy cases in which the sex is given, forty-one (58.6 per cent) of the patients being females and twenty-nine (41.4 per cent) males. In the second group, there are nine patients for whom the sex is given, five being females and four males.

Of the first group of tumors, twenty-two were located about the head, fifteen involving the brain and the others the cranial nerves. Ten were found in the neck, including one of the vagus nerve. In the second group there was one in the neck. There were eleven cases with involvement of the mediastinum, all in the first group. In the abdomen, retroperitoneally, and in the pelvis there were thirty-seven tumors in the first group and nine in the second, which shows a much greater incidence in the intermediate group in these locations. Of these tumors, there were ten in the suprarenals in the first group and four in the second. Six tumors were considered as subcutaneous, even though they involved some of the deeper-lying nerves. In the cases in which the side of the body on which the tumor occurred was stated, there were twenty-nine tumors on the left side and twenty-two on the right side. It has been commonly stated that there is a preponderance on the left side.

In the first group thirty-five patients were operated on. Twenty-two of these were children and twelve were adults, all of the latter

TABLE 1.—*Simple Ganglioneuromas*

Number	Author	Age of Patient	Site of Tumor	Comment
1	Perls	.....	Optic nerve (retrobulbar)	
2	Klebs	.....	Optic nerve	
3	Haenel	46 yr.	Dura on right side; two tumors	
4	Worcester	42 yr.	Left parietal lobe of brain	
5	Dumas	.....	Cerebrum	
6	Marchand	56 yr.	Gasserian ganglion	
7	Risel	20 yr.	Gasserian ganglion and cranial nerves; eleven tumors	Transition and young cells; small round cells
8	Schmincke	16 yr.	Right temporal lobe (retrobulbar)	Epileptiform seizures for 8 years
9	Pick and Bielschowsky	24 yr.	Medulla	
10	Achucarro	21 yr.	Cerebellum	
11	Robertson	24 yr.	Floor of third ventricle	Symptoms for 19 years
12	Berblinger	17 yr.	Septum pellucidum	
13	Greenfield	26 yr.	Tuber cinereum region	
14	Olivecrona	39 yr.	Right temporal lobe	
15	Olivecrona	Adult	Right frontal lobe	Young ganglion cells
16	Lhermitte and Duclos	.....	Cerebellum	
17	Bielschowsky	26 yr.	Ventricular walls of brain	Numerous tumors
18	Marinesco	.....	Infundibulum region	
19	Bally	.....	Pineal body	
20	Klebs	.....	Trigeminus acusticus	
21	Key	31 yr.	Left infra-orbital nerve	Successful operation
22	de Jong	20 mo.	Infra-orbital nerve	Successful operation
23	de Quervain	13 yr.	Left cervical sympathetic	Successful operation
24	Benda	Child	Right vagus ganglion (?)	Calcified areas
25	Glinski	10 yr.	Left cervical; first noticed at 7 months of age	Operated on successfully
26	Woods	32 yr.	Under right carotid sheath	
27	Freund	6 yr.	Right cervical	Operated on successfully; undifferentiated cells; not proliferating
28	Geymueller	5 yr.	Left cervical	Operated on successfully
29	Sommerfelt	36 yr.	Cervical; present 6 years	Operated on successfully
30	de Jong	Birth	Left cervical	Operated on successfully
31	Stout	2½ yr.	Right cervical; present since 5 weeks of age	Operated on successfully
32	Harbitz	22 yr.	Neck; present for 20 years	Operated on successfully
33	Loretz	35 yr.	Left thoracic segment; projected into spinal canal	
34	Borst	.....	Left thoracic segment	
35	von Rindfleisch	.....	Thoracic segment	Called hyperplastic ganglion
36	Tschistowitsch	12 yr.	Right thoracic segment	
37	Friedrich	73 yr.	Right thoracic segment	
38	Rosenson	8 yr.	Right side of mediastinum	Operated on successfully
39	Stout	2½ yr.	Right side of mediastinum; projected into spinal canal	Patient operated on and died
40	Brunner	19 yr.	Left side of mediastinum	Operated on successfully
41	Riggs and Good	4 yr.	Neck and mediastinum; symptoms for 22 months	Operated on; incomplete removal; relief for 16 months, then patient died
42	Crile	8 yr.	Left side of mediastinum; symptoms for 1 year	Operated on successfully
43	This paper (case 1)	5 yr.	Right side of mediastinum	
44	Weischselbaum	76 yr.	Left suprarenal medulla	Questionable evidence of proliferation
45	Chiari	.....	Suprarenal	
46	Schmidt	37 yr.	Left suprarenal	Operated on
47	Brüchanow	65 yr.	Left suprarenal medulla	
48	Ribbert	Adult	Suprarenal	
49	Ribbert	Adult	Suprarenal	
50	Oberndorfer	12 yr.	Left suprarenal	Some young cells
51	Hook	14 yr.	Right suprarenal	
52	Fabris	4 yr.	Left suprarenal	
53	Waszmund	26 yr.	Right suprarenal	
54	This paper (case 2)	4½ yr.	Attached to right kidney	
55	Busse	4 yr.	Retroperitoneal, in left side of pelvis	Operated on successfully
56	Glockner	38 yr.	Retroperitoneal, on left side of lumbar spine	Operated on successfuily
57	Ohse	5 yr.	Retroperitoneal, on left side of lumbar spine	Patient operated on and died
58	Braun	6½ yr.	Retroperitoneal, below the left kidney	Operated on successfully; young proliferating cells
59	Sato	31 yr.	Retroperitoneal, on left side of lumbar spine	Operated on successfully; small round cells and transition forms
60	Jones, H. M.	18 yr.	Retroperitoneal, on left side of lumbar spine; started at 5 years of age; rapid increase in size during last 2 months	Operated on successfully; some undifferentiated embryonic tissue

TABLE 1.—*Simple Ganglioneuromas—Continued*

Number	Author	Age of Patient	Site of Tumor	Comment
61	Peters	3½ yr.	Retroperitoneal, on right side of lumbar spine	Operated on successfully; undifferentiated cells, not proliferating
62	Geller	16 yr.	Right kidney	
63	Behan	19 mo.	Left lumbar spine; swelling present for 6 months	Operated on successfully
64	Auschütz	.....	Retroperitoneal about aorta	Operated on successfully
65	Gamma	60 yr.	Left side of abdomen	
66	Cappell	27 yr.	Retroperitoneal, right side	
67	Strada	23 yr.	Retroperitoneal, in pelvis	
68	Kopriwa	55 yr.	Left retroperitoneal	Operated on successfully; groups of embryonic lymphoid-like cells
69	Chiari	22 yr.	Retroperitoneal, in front of sacrum	
70	Cripps and Williamson	21 yr.	Retroperitoneal, in front of left side of sacrum	Operated on successfully
71	Benecke	25 yr.	Back of vagina	Some small cells believed proliferating
72	Schorr	18 yr.	Retroperitoneal, in pelvis	
73	Stoeckel	.....	In true pelvis	
74	Roman and Arnold	3 yr.	Retroperitoneal, in pelvis	Young neurogenic tissue
75	Newmann	14 yr.	Broad ligament	Operated on successfully
76	Krecke	55 yr.	Retroperitoneal, near pancreas; four tumors	Operated on successfully
77	Falk	16 yr.	Celiac ganglion region	Patient operated on and died
78	Patterson	9 yr.	In mesentery	Operated on successfully
79	Bland-Sutton	10 yr.	In mesentery; patient first operated on at 4 years of age	Operated on successfully
80	Poate and Inglis	30 yr.	Involving ileum and colon	Operated on successfully
81	Knaus	8 yr.	Sixty subcutaneous nodules	First noticed at 3 years of age
82	Kredel and Benecke	5 yr.	One hundred and sixty subcutaneous nodules	First noticed at 3 months of age
83	Hagenbach	38 yr.	Knee	
84	Krauss	.....	Eyelid	
85	Schultz	Birth	Scalp	Operated on successfully
86	Cushing and Wolbach	11 yr.	On back; of hour-glass type extending into spinal canal	Operated on successfully

TABLE 2.—*Intermediate Tumors*

Number	Author	Age of Patient	Site of Tumor	Comment
1	Dunn	3 yr.	Sphenomaxillary fossa	Operated on successfully; embryonic cells
2	von Fischer	Stillborn	Left cervical	Embryonic cells; immature ganglioneuroma
3	Küster	Adult	Suprarenal	Undifferentiated cells, not proliferating
4	Brossok	11 yr.	Right suprarenal; involved liver by continuity	Proliferating ganglion cells in lymph nodes
5	Berner	4½ yr.	Left suprarenal	Lymph nodes contained ganglion cells
6	Miller	16 yr.	Hilus of right kidney	Lymph nodes contained ganglion cells and lymphoid-like cells
7	Wegelin	20 yr.	Retroperitoneal below left kidney	Operated on successfully; incompletely differentiated ganglion cells and sympathoblasts
8	Beneke	10 yr.	Celiac ganglion	Patient operated on and died; lymph nodes contained ganglion cells
9	Adams	3 yr.	Abdominal to right of lumbar spine	Contained lymphoid-like cells
10	Jaffé	31 yr.	Left suprarenal	Contained undifferentiated cells
11	Rapp	4 yr.	Left side of abdomen	Infiltrated muscle tissue; no metastasis; contained glia cells; operated on successfully

making a complete recovery. The age of one patient who recovered was not given. Of the children, eighteen recovered and four died at the time of operation or shortly thereafter. One of the deaths was attributed to status thymicolymphaticus. In the second group, four patients were operated on, one adult and three children, with one death in a child. Summarizing, for the two groups there is a total of thirty-nine patients operated on with thirty-four recoveries and five deaths. It is seen that, even though some embryonic elements are present, removal of the tumor usually leads to recovery without recurrence of the growth or the development of metastasis. In Schultz' patient operation was performed on the second day of life. In Cushing and Wolbach's case, the patient was operated on at 1 year of age and again at 11 years of age, when the tumor was completely removed. Operation has proved successful for abdominal cases as well as for mediastinal growths. It is seen from the foregoing statements that in operable cases the prognosis is good, even though there is microscopic evidence of undifferentiated cells. Early operation would seem to be indicated, although malignant manifestations, such as metastasis in the intermediate type, seem to be slow. In some cases the tumors have been known to be present for years. In Macnaughton Jones' patient the tumor had not changed in size for several years; then in two months it began to grow rapidly, and on removal was found to contain embryonic cells. Whether these cells had just sprung into activity or whether failure to differentiate into ripe forms had just begun, one cannot say. Generally, ganglioneuromas are slow-growing.

Not much can be said about symptoms. The tumor itself rarely is the source of symptoms, but it causes them by pressure on adjacent organs and tissues.

As to treatment, operation seems to be the only cure. Roentgen therapy has been thoroughly tried, especially on Sommerfelt's patient, without any apparent result. There is no evidence that the tumors decrease in size spontaneously. Coley's toxin was used in Cushing and Wolbach's patient at the age of 1 year, before he came under their care, and when the tumor was considered to be a sarcoma. There was some change in the tumor, but this was described as coincidental.

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Pediatric Biographies

EUCHARIUS RÖSSLIN

?-1526

JOHN RUHRÄH, M.D.
BALTIMORE

Eucharius Rösslin, whose name appears variously as Röslin, Rössly, Roselin, Roessle and in the latinized form of Rhodion, first appears in written records in Freiburg in 1493. He lived there until 1504, when he gave up his citizenship and repaired to Frankfort-on-Main, where, in 1506, he was appointed *Stadtarzt* at 60 florins a year. In 1538, he went temporarily to Princess Katherina von Braunschweig und Lüneburg, to whom he dedicated his book. In 1513, he became *Stadtarzt* in Worms, and, in 1517, he returned to his old position in Frankfort with his salary increased to 70 florins. He died in 1526, according to the researches of the historian Baas.

Rösslin's book on obstetrics was the popular text of the time and for a century or more held sway, as will be seen by the numerous editions. It is largely made up of material derived from Soranus of Ephesus through the manuscript codices of Moschion, and much has been written on this subject. Further information may be had in the exhaustive articles by Gustav Klein (*Arch f. Gesch. d. Med.* **3**: 304, 1909-1910) and K. Baas (*ibid.* **1**: 429, 1907-1908). Rösslin's contribution to podalic version is of interest to obstetricians. The book appeared first in 1513 and went through 17 editions in German between that time and 1531. The "Ehestandarzeneibuch," edited by his son, continued it from 1526 to 1565 in 11 editions in German, and then the "Hebammenbüchlein" of Adam Lonicer kept it going in 10 more German editions, from 1562 to 1608. There were 12 Latin editions from 1532 to 1563, 8 in French from 1536 to 1586, 15 in English from 1540 to 1564, and the book also appeared in Danish, Spanish, Bohemian and Italian. It was plagarized by Walter Reiff in 5 more editions, altogether 99 editions, with 5 more referred to which Klein could not find, making a total of 104, and to this must be added Klein's reprint in 1910. Not a bad record.

A part of Rösslin's book, chapter X, is devoted to the care of the new-born; chapter XI to nursing and weaning and chapter XII to the diseases of the new-born. His teachings are largely taken from Avicenna, much in vogue at that time. He doubtless knew Metlinger's

book, and in a former paper I stated that I thought much was derived from Metlinger, but Rösslin does not quote so many of the ancient authorities. This pediatric part was considerably changed in various editions, and some, as the 1571 German edition, used the Metlinger text and so stated. The English translation by Jonas, afterward used by Raynalde in the "Birth of Mankind," as the English version of Rösslin is called, for many years served as a pediatric text. There are 36 short chapters covering the usual run of conditions as met with in pediatric practice. The following short excerpts may be taken as examples:

On Terrifying Dreams

Children may have terrifying dreams which come generally from overfilling so to help it do not allow it to go to sleep with a full stomach. And give it a little honey to lick so that it may digest in its stomach and pass out in the stool.

Item. Give every day the seventh part of an electuary named dyamuscum dyapliris and more healthy is theriac given with milk as Rhazes says.

When a Child Is Too Thin and Weazened

When the child falls away so that he is but skin and bone so that the child become sickly, let him be bathed in water in which the head and feet of a wether has been boiled until the flesh falls from the bone of its own accord and in this shall the child be often bathed. And when it has been bathed let it be well dried and then anoint it with this salve of fresh butter and oil of violets or rose oil, of each one ounce half an ounce of lard and an ounce of white wax. Melt these together and make a salve and with it smear the child daily after the bath from which the child will gain and fatten.

Item. Another salve for the same: Take white wax and lard and tallow and fresh butter, melt together and strain through a cloth and use like the above.

Tenasmus

There is also a disease of childhood called in Latin Tenasmon in which the child has a desire to go to stool but does nothing or little. This generally comes from cold. To help it take garden cress seeds and Roman kümmel seeds, of each equal parts, powder them well and temper with old butter and give it to the child to drink with cold water.

Item. Take turpentine and lay it on glowing coals, and let the fumes in his anus.

Item. Another one. Take Grecian tar called in Latin colofonia, lay it on glowing [coals] and let the fumes go in the child's hinderparts. [By allowing it under the bedclothes under which the child lies naked as later commentators add.]

Pediatrics in Art

BRAIN LESION

JOHN RUHRÄH, M.D.
BALTIMORE

A detail of the picture of "The Transfiguration."

Among the paintings of Raphael Santi (1483-1520) in which medical subjects are found, the boy in "The Transfiguration" is perhaps the most interesting. The painting was begun during the latter part of Raphael's life and remained unfinished at his death. DuBois Raymond, in a lecture in Berlin, 1890, called attention to the Magendie position of the eyes, as indicative of disease of the central nervous system. The boy's left hand is in a state of athetoid spasm. The photograph is by Alinari, from the original in the Vatican Gallery at Rome.

News and Comment

SOCIETY NEWS

American Committee, International Congress.—The following have been appointed as representatives on the American Committee for the Third International Congress to be held in London in 1933. Pediatric Section of the American Medical Association: Dr. John L. Morse, Boston; Dr. William Weston, Columbia, S. C., and Dr. H. F. Helmholz, Rochester, Minn. American Pediatric Society: Dr. C. G. Grulee, Chicago; Dr. A. Graeme Mitchell, Cincinnati, and Dr. C. A. Aldrich, Winnetka, Ill. American Academy of Pediatrics: Dr. Borden S. Veeder, St. Louis; Dr. J. Durand, Seattle, and Dr. Alfred F. Hess, New York. Society of Pediatric Research: Dr. L. Emmett Holt, Jr., Baltimore; Dr. Joseph Stokes, Jr., Philadelphia, and Dr. Charles F. McKhann, Jr., Boston.

American Pediatric Society.—At the meeting of the society at Rochester, Minn., on May *26*, *27* and *28*, the following were elected to membership: Dr. B. E. Bonar, Salt Lake City; Dr. Horton R. Casparis, Nashville, Tenn.; Dr. D. C. Darrow, New Haven, Conn.; Dr. George M. Lyon, Huntington, W. Va.; Dr. Francis Scott Smyth, San Francisco, and Dr. A. A. Weech, New York.

UNIVERSITY NEWS

Dr. Alfred F. Hess, professor of clinical pediatrics in the University and Bellevue Hospital Medical College, New York, has been elected a member of the "Deutsche Akademie der Naturforscher."

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

CERTAIN MONILIAS PARASITIC ON MAN: THEIR IDENTIFICATION BY MORPHOLOGY AND BY AGGLUTINATION. RHODA W. BENHAM, J. Infect. Dis. **49**: 183 (Sept.) 1931.

In this important paper, the author tries by many methods to distinguish between the several monilias obtained from various sources as well as from the American Type Culture Collection. The fact is important that the thrush parasite can be recognized and differentiated from other related forms by its cultural response and morphologic appearance. The author concludes that for the present, at least, many of the yeastlike organisms found in erosio interdigitalis, chronic paronychias, perlèche, certain cases of superficial glossitis and other dermatoses should be classed as thrush. Of thirty strains of monilias tested for virulence, nineteen were pathogenic for rabbits but not for rats and monkeys. Benham concludes that agglutination reactions in conjunction with other studies serve as the best means for the identification of these yeasts.

TOOMEY, Cleveland.

THE INFLUENCE OF PUS AND BLOOD ON THE ACTION OF BACTERIOPHAGE. MARTHA APPLEBAUM and WARD J. MACNEAL, J. Infect. Dis. **49**:225 (Sept.) 1931.

A patient with multiple boils and a positive blood culture for the staphylococcus died even though treated with a bacteriophage. Many detailed experiments are reported, and the authors conclude that pus exercises an inhibitory action on the antistaphylococcus bacteriophage. In their comment, they wisely call attention to the fact that the indications for surgical drainage are "hardly at all altered by the advent of bacteriophage" though the latter may be used after the purulent material is removed at operation.

TOOMEY, Cleveland.

MYCOBACTERIUM: ERGOSTEROL CONTENT OF CERTAIN SPECIES AND EFFECT OF ERGOSTEROL ON THEIR GROWTH. PAUL S. PRICKETT and O. N. MASSENGALE, J. Infect. Dis. **49**:297 (Oct.) 1931.

Though Bacillus tuberculosis has a high lipoid content, 23.78 per cent (Anderson), no ergosterol was found by the author, thus confirming Anderson and Chargoff's observations. Uninactivated ergosterol added to the medium used stimulated growth and pigment-formation, while activated ergosterol stimulated pigment production but not growth, and in higher concentrations retarded growth.

TOOMEY, Cleveland.

THE PYROGENIC REACTION TO CONCENTRATED ANTIPNEUMOCOCCUS SERUMS, WITH RESPECT TO CERTAIN SERUM CONSTITUENTS: SECOND PAPER. LLOYD D. FELTON and GLADYS KAUFFMANN, J. Infect. Dis. **49**:337 (Oct.) 1931.

The authors tried to ascertain the causative factor for chills by analyzing various chill-producing specimens of pneumococcic antibody solution. They tentatively concluded that the chill reaction was associated with a water-insoluble protein slightly more acid than that with which the protective substance is found. The chill-producing lots have a slightly higher content of phosphorus and lipoid, and contain more ammonia, more nonprotein nitrogen and more precipitable material at certain p_H values than nonchill-producing lots. The authors promise more data in future papers on the precipitable material.

TOOMEY, Cleveland.

INFLUENCE OF ARTIFICIAL FEVER ON THE COURSE OF EXPERIMENTAL POLIOMYELITIS. CLAUS W. JUNGEBLUT and NICHOLAS KOPELOFF, J. Infect. Dis. **49**:348 (Oct.) 1931.

The authors tried various modifications of Wagner-von Jauregg's artificial fever therapy in an endeavor to prevent experimental poliomyelitis. They conclude that "as regards poliomyelitis, the production of a sufficiently intense fever to bring about destruction of the virus in vivo is not possible within a safe zone of raised temperature."

TOOMEY, Cleveland.

BACTERIOPHAGE ADAPTATION. PAUL J. BEARD, J. Infect. Dis. **49**:367 (Nov.) 1931.

The author gives a complete and well analyzed bibliography on the subject of the adaptation of bacteriophage. He states that the opinion of those who hold this possible is based on errors of technic and interpretation. In his experiments, he obtained no evidence of adaptability.

TOOMEY, Cleveland.

THE DIPHTHEROID PHASE OF STREPTOCOCCI. LLOYD B. JENSEN and HERSCHEL B. MORTON, J. Infect. Dis. **49**:425 (Nov.) 1931.

The authors isolated a bacterial strain from the urine of a patient suffering from cystitis, and were able to mutate the bacteria at will from a diphtheroid to a streptococcal form. They believed that the diphtheroid form represented one state of the streptococcus. In addition, they found that the bacteria were avirulent for rabbits in the diphtheroid phases but virulent in the streptococcal forms.

TOOMEY, Cleveland.

LETHAL TEMPERATURES FOR PORCINE STRAINS OF BRUCELLA ABORTUS, WITH SPECIAL REFERENCE TO PASTEURIZATION. RUTH A. BOAK and C. M. CARPENTER, J. Infect. Dis. **49**:485 (Dec.) 1931.

These authors state that pasteurization of milk (heating for from twenty to thirty minutes at from 142 to 145 F.) destroys the most virulent strains of Brucella abortus.

TOOMEY, Cleveland.

INTERSTITIAL PERIPHERAL NEURITIS IN EXPERIMENTAL POLIOMYELITIS, WITH NOTES ON THE NATURE OF THE FIRST PATHOLOGIC CHANGES IN THE SPINAL CORD. A. JORDI, J. Infect. Dis. **49**:530 (Oct.) 1931.

This is an excellent article showing that round cell infiltration occurs in nerve trunks. From Jordi's observation, with which we can agree on the basis of other experiments, the first manifestation of the virus is the necrosis of cells and not the interstitial inflammation, as suggested by older authors.

TOOMEY, Cleveland.

A CONTRIBUTION ON THE DISTRIBUTION OF CALCIUM CONTENT IN BLOOD OF CHILDREN. M. SOKOLOVITCH, Brit. J. Exper. Path. **12**:150 (June) 1931.

The calcium content of whole blood, blood serum and red blood corpuscles was studied in five normal children and two children suffering from tetany with rickets. The red blood corpuscles of the five normal children were practically devoid of calcium, but the corpuscles of the two children with tetany contained an appreciable amount, suggesting that there is some shifting of the calcium from the blood serum into the corpuscles in this disease.

KUGELMASS, New York.

THE RELATION BETWEEN THE CALCIUM AND INORGANIC PHOSPHORUS CONTENT OF SERUM AND THE SYMPTOMS OF PARATHYROID TETANY. A. VON BENZNAK, Biochem. Ztschr. **236**:362, 1931.

It is shown that the rise in the inorganic phosphorus of the blood during parathyroid tetany is due, at least in part, to a hydrolysis of the phosphocreatine of the contracting muscles. Owing to the absence of the parathyroid hormone, calcium disappears from the blood and accumulates in the bones. This causes a shift in the ionic ratio $(K^+—Na^+)/Ca^{++}$, which increases the muscular instability and leads to twitching of the muscles. These twitches induce cleavage of the phosphagen, discharging the free orthophosphoric acid into the blood stream. The fact that the elimination of phosphorus is diminished in the absence of the parathyroid hormone also contributes to the rise in the phosphorus content of the blood, and this in turn produces a further lowering of the blood calcium. The three cardinal symptoms of tetany, namely, a low calcium and a high phosphorus content and tetanic contractions, form a sort of vicious circle.

KUGELMASS, New York.

THE IRON CONTENT OF THE BLOOD OF INFANTS. I. A. KOTIKOFF, Jahrb. f. Kinderh. **132**:180 (July) 1931.

Using the Foweather method with 0.5 cc. of whole blood from the heel, the author found that the iron content fell from 61.8 mg. per hundred cubic centimeters in the first month to 43.4 mg. in the second, reaching a minimum of 38.7 mg. in the ninth. Vegetables in the diet caused an immediate rise. Seasonal variation was from a maximum of 47.6 mg. in April to a minimum of 39.4 mg. in September. Long-continued illness caused a marked fall.

CLAUSEN, Rochester, N. Y.

LIPASE IN THE LUNGS OF THE HUMAN FETUS AND THE NEW-BORN CHILD: SUPPLEMENT; OTHER INTESTINAL LIPASES. T. TACHIBANA, J. Kinki, Gynec. Soc. **12**:10, 1929.

Lipase was detected in fetal lungs from the fourth month on. It increases with subsequent development. In the liver and in the intestines, lipases appear earlier. The lipases of the stomach and kidneys correspond to the lipase of the lungs. No lipase is found in the skin, gallbladder or brain of the fetus or new-born child.

KUGELMASS, New York.

Nutrition

THE EFFECT OF DIFFERENT PERCENTS OF PROTEIN IN THE DIET: I. GROWTH. II. SPONTANEOUS ACTIVITY. III. INTAKE AND EXPENDITURE OF ENERGY. IV. REPRODUCTION. JAMES R. SLONAKER, Am. J. Physiol. **96**:547 and 557; **97**:15 and 322, 1931.

1. Five diets that were similar except for the protein content, which was 10, 14, 18, 22 and 26 per cent, respectively, were fed to rats. For the best growth the amount of protein should be slightly in excess of 14 per cent. A deviation of 4 per cent, more or less, produced no serious results. As the protein increased beyond the optimum there was a progressive retardation in growth. 2. A diet containing between 14 and 18 per cent protein is best suited to the albino rat for maximal spontaneous running. 3. Five groups, each comprising ten young albino rats, were fed complete synthetic diets that contained 10, 14, 18, 22 and 26 per cent protein, respectively, but were otherwise as nearly alike as possible. Between 14 and 18 per cent protein results in the greatest efficiency in maximal growth, spontaneous activity, reproduction and life span. During the growing period the diets containing the larger percentage of protein produced the greater

percentage of gain in weight. 4. Success in reproduction and in rearing young in rats was greatest on a diet containing 14 per cent protein, followed by 10, 18, 22 and 26 per cent.

KUGELMASS, New York.

GROWTH AND DEVELOPMENT. ROBERT A. STRONG, Arch. Pediat. **48**:567 (Sept.) 1931.

The author reviews some of the many different factors that influence growth and development. The article is of a general nature, and for this reason cannot be adequately abstracted.

WADDELL, University, Va.

PRESENT DURATION OF BREAST FEEDING. EDWARD J. LAMB, California & West. Med. **35**:297 (Oct.) 1931.

The series studied consisted of 1,000 well babies under the author's care over a period of two years, the mothers being intelligent Americans of at least moderate financial status. The series compares favorably with similar social groups reported on by other authors eight or ten years ago, and it may be concluded that the duration of breast feeding has not decreased during the last two decades. The babies fed on artificial milk formulas showed no serious deviations from the normal development that regularly follows adequate breast feedings, the success of the formulas being attributed to the character of the milk and the intelligent cooperation of the mothers.

DICKEY, San Francisco.

VITAMINS C, D AND E (IN AVOCADOS). L. WEATHERBY, California Avocado A. Yearbook, 1930, p. 100; Exper. Station Rec. **64**:587, 1930.

Amounts of avocado as low as 0.5 Gm. daily prolonged the life of guinea-pigs over that of controls on the scorbutic diet alone, but amounts up to 5 Gm. daily did not prevent scurvy. On 5 Gm., resort had to be made to forced feeding; larger amounts were not tested. These findings indicate that the avocado contains a small amount, but is not a good source, of vitamin C. The avocado contains vitamin D in liberal quantities, although both the rosary and the line tests indicated rickets on doses as high as 5 Gm. in curative tests and mild rickets on the same dosage in preventive tests. The results of tests for blood phosphorus were normal, but other recent observations have indicated that this is sometimes the case in well defined rickets. The results with 2.5 cc. of avocado oil were normal for the rosary and blood phosphorus tests, as traces of rickets were shown in the line tests. Five grams of avocado or 715 drops of oil were the minimum doses found effective in producing cures in the female rats fed on the Evans sterility diet. Cures were not effected in the males, and preventive measures were not tested.

KUGELMASS, New York.

INVESTIGATIONAL WORK IN CEREAL CHEMISTRY. FRANK T. SHUTT, Canad. Dept. Agr., Rept. Dominion Chemist, 1930, p. 40.

Analyses were made of the Reward variety of wheat at two day intervals during a period of twenty-six days from the "late milk" to the "firm dough" stage. The percentage of protein (dry matter basis) decreased markedly from the first to the fifth cutting, and then increased for the next two cuttings, after which it was approximately constant. The percentage of ash decreased with the development of the kernel, being approximately constant from the seventh cutting. The protein and ash in the flour followed the same trends as in the kernel. The protein and ash contents of the flour averaged 0.75 and 1.2 per cent, respectively, lower than those of the corresponding wheat. The protein and ash contents of a large number of samples, comprising some fifty varieties of wheat grown in the prairie provinces, are tabulated.

KUGELMASS, New York.

A Study of the Enzymes of Stools in Intestinal Intoxication. F. G. Banting, S. Gairns, J. M. Lang and J. R. Ross, Canad. M. A. J. **25**:393 (Oct.) 1931.

The authors studied a series of cases to determine the variations in enzyme activity in intestinal toxemia in infants. Details are given as to the methods employed. The authors' conclusions were that the stools of normal infants contain large amounts of trypsin, amylase and lipase. The trypsin content of the stools of infants suffering from intestinal intoxication was decreased in proportion to the severity of the condition. Bronchopneumonia, mastoid or other focal conditions complicating the intestinal toxemia caused the clinical condition to be worse but without a corresponding lowering of the trypsin curve. Amylase and lipase were also studied and were found to vary. In general, a low trypsin content was accompanied by a low amount of amylase and lipase, but sometimes there was a high trypsin content, with the amylase and lipase content either high or low. The authors conclude that in intestinal intoxication the pancreas fails to produce its normal quantity of enzymes. The original theory that the action of the enzymes was inhibited by raw serum was not proved.

Moore, Omaha.

Vitamin B Content of Vegetables: I. Distribution of Vitamin B in the Carrot. II. Effect of Sunlight on the Vitamin B Content of Lettuce, Kohlrabi and Tomatoes. III. Effect of Storage on the Vitamin B Content of Carrots. M. C. House, P. M. Nelson and E. S. Haber, Iowa Agric. Exper. St. Res. Bull. 120, 1930, p. 333.

Determinations of the vitamin (F and G) content of the core, flesh and skin of Chantenay carrots by the Sherman-Spohn method gave statistically significant differences in the gain in weight of experimental animals on the same dosage of different parts of the carrot. The skin or periderm contained more vitamin B than the cortex (flesh), and the latter more than the core (xylem). The authors conclude that from a nutritional point of view carrots should not be peeled or scraped unless such a procedure is absolutely necessary to make them palatable. For the nutrition worker, the data stress the importance of careful sampling in all determinations of the vitamin content of foods. Lettuce of the Grand Rapids variety, white Vienna kohlrabi and Bonny Best tomatoes were grown outdoors for eight weeks. The following winter the same varieties were grown in the greenhouse under as uniform growing conditions as possible. The vitamin B tests showed no significant differences between the garden-grown and the hothouse-grown vegetables, although insufficient data were obtained for definite proof. Kohlrabi, which had not been previously tested for vitamin B content, proved to be a relatively good source, 4 Gm. daily sufficing for fairly satisfactory growth. Carrots showed no appreciable loss in vitamin B on storage in a cellar for five months.

Kugelmass, New York.

Acute and Habitual Vomiting in Infants, with Reports of Five Illustrated Cases. Esther B. Hardisty, M. J. & Rec. **134**:219 (Sept. 2) 1931.

Dr. R. H. Dennet classified vomiting under the headings of acute and habitual. The cause of acute vomiting may be indigestible food, unfit for the infant, and acute infectious gastro-enteritis. He defined habitual vomiting as vomiting that may occur every day for at least a week and often for many weeks. The author points out that vomiting is one of the clinical signs of many conditions. Marriott has stated that vomiting from overdistention of the stomach can be remedied by giving a more concentrated feeding. Fat intolerance often predisposes to vomiting. Thickened feedings are often well tolerated in vomiting infants. Dried

milk often is well tolerated, which may be due to the fact that its fat content is low. The danger of dehydration is always present when the vomiting continues over many days. The article is accompanied by the histories of five cases.

WILLIAMSON, New Orleans.

BREAST NURSING VS. ARTIFICIAL FEEDING. O. B. WEINSHANK and M. L. FURMAN, M. J. & Rec. **134**:*222* (Sept. 2) 1931.

Cow's milk was shown by Russian biologists to be insufficient for the proper growth and development of the infant. Artificially fed infants are more susceptible to tuberculosis. The authors appeal to members of the medical profession to educate mothers regarding infant nutrition and to insist on breast feeding. The mothers should be warned against dieting, and its consequences should be explained.

WILLIAMSON, New Orleans.

EFFECT OF FEEDING DIFFERENT AMOUNTS OF CALCIUM AND PHOSPHORUS UPON THE GROWTH AND DEVELOPMENT OF DAIRY ANIMALS. H. O. HENDERSON and C. E. WEAKLEY, JR., West Virginia Agric. Exper. St. Bull. 231, 1931, p. 56.

Four groups of eight calves each were fed rations similar in nutritive value but varying in the amounts of calcium and phosphorus. The proportion of calcium and phosphorus in the ash of bone remained approximately the same regardless of the ration. Analyses of the ribs, femurs and humeri gave the same general results. In the group fed the normal ration, the analyses of the bones showed a composition fairly representative of the bones of normal cattle at various ages.

KUGELMASS, New York.

PROTEIN ASSIMILATION INFLUENCED BY LACTATION. H. T. PARSON and I. STEVENSON, Wisconsin Exper. St. Bull. 410, 1930, p. 21.

In rats the act of suckling the young was followed by an increase in the concentration of urea in the blood of the mother regardless of the time elapsing since food had been eaten. There was no correlation between this increase in the urea content of the blood and the amount of milk lost. Experiments to check these observations were conducted on lactating cows, dogs, guinea-pigs and rabbits. With cows no increase in the urea content of the blood was observed, but with rabbits and guinea-pigs there was a slight increase. Cooked beef liver was slightly superior to casein as a source of protein for lactation in rats. Egg albumin was very unsatisfactory, and no young were raised when raw egg albumin served as the sole source of protein for the mother. Somewhat better, but far from satisfactory, results were secured with cooked albumin.

KUGELMASS, New York.

EFFECT OF VIOSTEROL ON BONE. R. SOEUR, Arch. internat. de méd expér. **6**: 365, 1931.

The administration of massive doses of viosterol is toxic; it embarrasses the general state of the animal and can produce rapid death. As shown by other investigators, these conditions are closely allied with calcium metabolism, producing intensive mobilization of calcium with a negative balance in the bones. The blood calcium tends to become elevated, and there results in various organs (heart, arteries, veins, etc.) abnormal storage depots of calcium. This mobilization of calcium is produced at the expense of the bone. It is the latter that is the subject of the present study. Using young and adult guinea-pigs and also adult rats, we have confirmed the observations of previous workers, concerning toxicity, the blood calcium and phosphorus values and abnormal calcification. We have studied the bones from a standpoint of pathologic anatomy. In the ribs, vertebrae, skull and long bones we have observed the following: the reabsorption of bone with

resulting fractures, abnormal phenomena in the bone marrow, manifested by intensive vascularization and aseptic necrosis and arrest in the osteogenic activity in young animals. We have obtained microscopic pictures absolutely different from those produced by the administration of parathyroid extract (generalized bony fibrosis). It is logical for us to suppose that viosterol does not act by exciting the parathyroid gland, and that the action in large doses is simply a toxic effect.

AUTHOR'S SUMMARY.

THE NEM SYSTEM: ITS PRINCIPLES AND ITS APPLICATION IN INFANT FEEDING. G. PATEY, Arch. de méd. d. enf. **34**:645 (Nov.) 1931.

This is an exhaustive discussion of the system created by the late Professor Pirquet, whose attempt to formulate a more specific basis of nutrition through a new unit of measurement has not been widely approved. Tables for the determination of the ration at different periods are concluded with a summary in which the author finds much to recommend this method in both health and disease.

AMESSE, Denver.

MAGNESIUM AND EXPERIMENTAL RICKETS. G. MOURIQUAND, A. LEULIER and ANDRÉ ROCHE, Compt. rend. Soc. de biol. **107**:676 (June 19) 1931.

In line with the observations on decalcification produced by strontium experimentally in rickets by Lenhart, Shipley and Park, Hess and other investigators, the authors studied the effect of adding 2 per cent magnesium carbonate to a rachitic diet in young rats. The animals lost weight more rapidly, and the clinical as well as the roentgenographic evidences of rickets were produced much more rapidly than in the control series. The results warrant the conclusion that magnesium and strontium have a similar decalcifying action in rachitic animals.

WAHL, Cleveland.

HYPERCALCEMIA FROM EXCESSIVE ULTRAVIOLET IRRADIATION. A. B. MARFAN and H. CORLEUCOURT, Nourrisson **19**:273 (Sept.) 1931.

In a girl aged 13 years with congenital syphilis and idiocy from early infancy subacute rickets developed with marked genu valgum and tetany. Owing to a prolonged feeding difficulty, she weighed only 35 pounds (16 Kg.). Roentgen examination revealed typical bony changes. Analyses of the blood showed a low calcium content (8.1 mg.) and a hypophosphatemia. Treatment with exposures to the ultraviolet radiations of a mercury quartz lamp at a distance of 80 cm. was begun. The length of time for each exposure was gradually increased up to thirty minutes. Daily exposures for twenty days were followed by a fifteen to twenty day period of respite. Later the exposures were given every second day. The symptoms of tetany and the signs of rickets were quickly ameliorated. The exposures were continued over a period of eighteen months—in all, 180 exposures were given, totaling about seventy hours. At about this time an analysis of the blood showed a slight hypercalcemia (12.8 mg.). A severe enterocolitis developed; the stools contained blood, mucus and many enteroliths. The intestinal calculi varied in size from that of a pea to that of a small nut. There also developed subcutaneous calcified nodules under the skin of the abdomen. There was no generalized infiltration of the skin (scleroderma). The patient died of the progressive cachexia. There was no autopsy.

MCCLELLAND, Cleveland.

ACCESSORY FOODS FOR THE INFANT AGED FROM SIX TO ELEVEN MONTHS. O. CODET, Progrès méd., Oct. 17, 1931, p. 1781.

The author introduces the fine cereals at 6 months, vegetable soup at 7 months, potatoes at 9 months, other vegetables and fruits at 10 months, eggs

at 11 months and meat at 12 months. The principal difference from the American dietary is the introduction of ripe cheese, such as Holland cheese, at 9 or 10 months. The author does not advocate fresh fermented cheese, such as Brie or Camembert.

SANFORD, Chicago.

AN APPLE DIET IN DIARRHEAL DISTURBANCES IN INFANTS. G. POPOVICIU, Rev. franç. de pédiat. **7**:473, 1931.

The author had good success with Moro's apple diet in parenteral disturbances, especially those of infectious origin. He reports two cases in detail, one of bronchopneumonia and the other of marasmus. Even with toxic symptoms it may be necessary to repeat the course of treatment at short intervals. The discovery of such a simple method of treating the grave parenteral diarrheas is of considerable importance.

SANFORD, Chicago.

THERAPEUTIC DEDUCTIONS ON THE CHLORINE, UREA AND ALKALINE RESERVE IN INFANTILE DEHYDRATION. G. PHELOZOT, Rev. franç. de pédiat. **7**:560 (Oct.) 1931.

The author established normal values in eleven infants, and then divided the pathologic cases into three groups. In the first group, that of digestive disturbances without infection, there were three cases of intestinal occlusion and eight of pyloric stenosis showing a marked chloropenia. In eight cases of dyspepsia without vomiting and diarrhea the blood was normal, while in three cases with diarrhea and vomiting the chlorine content was slightly lowered and the urea raised. In eight premature infants with dyspepsia and vomiting, the chlorine was markedly lowered. The second group contained cases in which dehydration was induced experimentally. In six cases the urea content was increased, the chlorine was lowered and the alkali reserve was lowered, inversely proportional to the amount of chlorine in the organism. The third group dealt with dehydration in infections. In nine cases of respiratory infections there was chloride retention, and in six other infections there was a lowering of chlorides; in three cases of dysentery there was a marked lowering. Phelozot concludes, therefore, that in dehydration the diet should be simple, reenforced by oral or subcutaneous injections of some chlorine substance, such as 7 per cent sodium chloride or Ringer's solution.

SANFORD, Chicago.

IRON IN THE NUTRITION OF INFANTS: I. A METHOD FOR THE ANALYSIS OF SMALL QUANTITIES OF IRON IN ORGANIC SUBSTANCES. A. WALLGREN, Rev. franç. de pédiat. **7**:596 (Oct.) 1931.

The author outlines a method of analysis for iron, which consists of melting the substance to be tested in a platinum capsule and of dissolving the residue in dilute hydrochloric acid. The solution is neutralized with ammonia and precipitated with nitroso-β-naphtol. The precipitate is dissolved in distilled water and potassium iodide added. Phenol is added, and the iodine is liberated in a solution of sodium thiosulphate. The titer of this solution is determined with a known solution of iron. This method is applicable to solutions of iron of more than 0.05 mg. It yields uncertain results with quantities below 0.025 mg.

SANFORD, Chicago.

THE ACTION OF THE VISUAL PSYCHIC REFLEX AND OF SUCKING ON THE GASTRIC SECRETION OF INFANTS. ANNA MARIA DORDI, Riv. di clin. pediat. **29**:791 (Sept. 15) 1931.

On a group of infants from 8 to 17 months of age, the following experiment was performed: A catheter was passed into the stomach, and approximately fifteen minutes later a sample of the gastric juice was withdrawn by a syringe.

Then the baby was either shown its accustomed feeding or given a rubber nipple to suck. After approximately ten minutes, another sample of gastric juice was withdrawn. In both instances, the gastric juice had become more acid and relatively richer in pepsin. These observations demonstrate that the use of a rubber "pacifier" may be useful, especially in cases of insufficiency of the digestive function of the stomach.

HIGGINS, Boston.

RICKETS AND VITAMINS. MARTINEZ VARGAS, Med. de los niños **32**:169 (June) 1931.

Rickets probably results from the lack of some vitamin in the food. This vitamin deficiency is more likely to occur in an infant on artificial food. The author reports a case in a child brought to his clinic at the age of 2 years. The child started to have convulsions at the end of the first month; these became progressively worse until it was having about thirty each day. The baby had been on breast milk, but was receiving cow's milk about the time the convulsions started. The cow's milk probably was lacking in the antirachitic agent that evidently was supplied by the mother's milk.

DWYER, Kansas City, Mo.

THE DETERMINATION OF THE ALUMINUM CONTENT OF FOODSTUFFS. K. B. LEHMANN, Arch. f. Hyg. **106**:309, 1931.

The author studied the aluminum content of fruits, cereals, vegetables, animal tissues and other materials used as foods. Tables give the results of the author's findings as well as those of previous investigators in this field. The aluminum content ranged from 0.13 mg. per hundred grams of the dry substance in egg-white to 7.2 mg. in beef.

GLASER, Rochester, N. Y.

ALLEGED INTOXICATION DUE TO THE PREPARATION OF FOOD IN ALUMINUM VESSELS. K. B. LEHMANN, Arch. f. Hyg. **106**:336, 1931.

The author critically reviewed cases of reputed poisoning due to the use of food prepared in aluminum vessels. He concluded that there was no real evidence that such poisoning had occurred, and that there was no valid reason to oppose the use of aluminum cooking utensils.

GLASER, Rochester, N. Y.

EFFECTS OF A RAW VEGETABLE DIET AND OF A MEAT DIET. HEINRICH WILLI, Deutsches Arch. f. klin. Med. **168**:156, 1930.

A vegetable diet of high caloric and low sodium chloride content was disagreeable when continued for ten weeks. A diet consisting mainly of meat was endured for fourteen days, but was equally disagreeable. On the raw vegetable diet, body weight decreased 2,750 Gm.; on the meat diet it increased 1,600 Gm. Absorption through the intestinal wall was much more marked in subjects on the meat diet. There were no abnormal variations in basal metabolism. The mineral balance during the diet with a low sodium chloride content was positive in spite of considerable loss in the feces; doses of 10 Gm. of sodium chloride taken during this time were not eliminated until after four days. A definite relation was observed between the excretion of organic acids and the H-ion concentration. On the raw vegetable diet the urine became strongly alkaline, and there was a marked increase in the amount of organic acid excreted; this supports the view that the increased elimination of organic acids in alkalosis is a reserve mechanism. The excretion coefficient for the organic acids is reciprocal to that for nitrogen. Throughout the test on both forms of diet there were no abnormal changes in the chemical composition of the blood.

KUGELMASS, New York.

THE GAS METABOLISM OF HEALTHY CHILDREN, WITH SPECIAL REFERENCE TO THE SPECIFIC DYNAMIC ACTION OF THE DIET. M. DE BRUIN, Jahrb. f. Kinderh. **132**:257 (Aug.) 1931.

Using the apparatus of Dusser de Barenne and Burger in children from 4 to 10 years of age, the author found the basal metabolism somewhat higher than the standard American figures. A specific dynamic action followed the test breakfast of 0.33 liter of milk. There was so much scattering in the results that no conclusions could be drawn with reference to the effect of age. The respiratory quotient was most variable, and was usually highest just before or during the greatest heat production. The author is most critical of his results.

CLAUSEN, Rochester, N. Y.

EXPERIMENTAL RICKETS IN THE RAT: VI. THE EFFECT OF IRRADIATED ERGOSTEROL AND HEATED IRRADIATED ERGOSTEROL ON SERUM PHOSPHATE. G. POPOVICIU, Jahrb. f. Kinderh. **132**: 286 (Aug.) 1931.

Irradiated ergosterol, heated and again irradiated, given in large doses raises the serum phosphate content in normal rabbits, and can also raise the "phosphatemic curve" following the administration of phosphate by mouth. This effect is associated with the toxic activity of the preparations, and not with their antirachitic potency. Consequently, such procedures are not suitable for the assay of antirachitic preparations.

CLAUSEN, Rochester, N. Y.

THE DELAYED HEALING OF FLORID RICKETS RESULTING FROM CHRONIC INFECTION. BRAINA CHAIT, Monatschr. f. Kinderh. **51**: 32, 1931.

The author presents a review of the recent literature on rickets, case reports, x-ray pictures and temperature curves leading to the following conclusions: 1. The healing of rickets occurs in from four to six weeks with specific treatment (viosterol). 2. In many cases, in spite of specific or light therapy, the healing was greatly delayed. At this time the infants were suffering from chronic febrile infections, nasopharyngitis, grip or furunculosis. 3. On the basis of these observations, the author believes that the most probable explanation of delayed healing in spite of specific treatment is that it is due to the infection. 4. Even the mildest infection, if it recurs frequently, is much more important in delaying the healing than a brief acute infection.

GERSTLEY, Chicago.

THE INFLUENCE OF THE TEMPERATURE OF THE FOOD ON THE NURSLING. MARGARETE HERRMANN, Monatschr. f. Kinderh. **51**:49, 1931.

The work was undertaken because the author believed that the influence of the temperature of the milk formula on the infant's nutrition had not been sufficiently studied. She varied the temperature of the bottle in a series of cases and found that ordinary variations had little effect on the infant. When the milk became definitely cool, i. e., between 20 and 30 C., some of the infants reacted with colic and diarrhea. The author believes that the ordinary measures taken by a good nurse are a sufficient safeguard for the child, but warns against overlooking this factor when babies are outdoors on a cool day.

GERSTLEY, Chicago.

PARALLEL INVESTIGATIONS WITH RAW AND STERILIZED BREAST MILK IN PREMATURE INFANTS. MARIE ELISE KAYSER, Monatschr. f. Kinderh. **51**: 199 (Oct. 31) 1931.

During the last four and a half years, Dr. Kayser has used about 10,000 liters of sterilized breast milk. In view of the fact that some objection has been raised to the boiling of breast milk, she reports that the children thrived as well on breast milk that had been boiled for twenty minutes as on the unboiled milk. There was no difference in the weight curves; there was no difference in the

digestion and stools; there seemed to be no difference in the resistance to mild infections. She does not advocate boiling breast milk except when there are definite indications.

GERSTLEY, Chicago.

THE SOURCE OF MINERALS DEPOSITED IN HEALING RICKETS. HIMA STOLZBERG, Monatschr. f. Kinderh. **51**:205 (Oct. 31) 1931.

To determine, if possible, the source of minerals deposited during the healing of rickets, or at any rate to determine the mode of action of the various procedures used in treatment, the author performed experiments on the calcium and phosphorus metabolism in litters of rats on different diets and different forms of treatment. He found the calcium and phosphorus content of bones to be identical in normal rats and in those treated with ultraviolet rays and given a rachitic diet. In severe rickets the calcium and phosphorus content of bones was decidedly diminished and did not come to the normal level even during the healing period. There was little difference in the calcium and phosphorus content of the organs of any of the rats, rachitic or nonrachitic, reckoned on 100 Gm. of dry substance. However, the bones and viscera of the rachitic and the recovering rats were richer in water than those of normal animals. As there was no diminution in the calcium and phosphorus content of any organ, the author reasons that the deposits of these minerals in the bones during healing could not have been taken from the organs. He concludes that there must be a better utilization of the calcium and phosphorus in the diet due to the treatment with ultraviolet rays.

GERSTLEY, Chicago.

AN UNDESCRIBED DIASTASE IN BREAST MILK. H. SCHLACK and W. SCHARFNAGEL, Monatschr. f. Kinderh. **51**:273 (Nov.) 1931.

The authors made the following interesting observation: Two cubic centimeters of uncooked breast milk is added to a thick solution of cornstarch (6 Gm. in 100 cc. of water). In from one-quarter to one-half hour, the mixture becomes fluid. Cooked breast milk does not give this result. A solution prepared with raw breast milk, however, remains fluid even if it is cooked later. The addition of 2 cc. of raw cow's milk to the original cornstarch mixture does not cause any change in the viscosity of the solution. These experiments were repeated with the milk of twelve different women. The diastase affects also the starches in potato, wheat and rye, but is more active on the purified starches, which are not protected by the cellulose and albumin substances of the raw grain. The authors suggest that this observation can be of use in differentiating breast milk from cow's milk. The presence of this diastase in breast milk is probably a provision by nature to compensate for the lack of ptyalin in the saliva of new-born infants. This diastase must also be remembered when thick cereal gruels are used. The use of breast milk in such feeding will probably liquefy the gruel rapidly.

GERSTLEY, Chicago.

PROPHYLAXIS OF RICKETS WITH IRRADIATED MILK. B. ESSIG, München. med. Wchnschr. **78**:273 (Feb. 13) 1931.

Irradiated skimmed milk is not effective in the prevention or cure of rickets. Irradiated whole milk is a good antirachitic agent.

BRAHDY, Mount Vernon, N. Y.

INCREASE IN WEIGHT OF CHILDREN WITH INACTIVE TUBERCULOSIS TREATED IN THE OPEN AIR IN THE CITY. W. KORNFELD and H. SCHÜLLER, Ztschr. f. Kinderh. **51**:340, 1931.

The increase in weight of 600 children who were being treated in the open air ward of the Children's Hospital at Vienna because of inactive tuberculosis was studied. If unselected children were divided on admission into large groups

of the same size, only proportionately small and irregular variations of the average gain in weight appeared. On the other hand, if one compared groups selected according to definite biologic points, there appeared many definite phenomena. In general, the girls showed a greater relative increase in weight than the boys, older children greater than younger, children at first underweight greater than children at first nearly normal or overweight. Exceptions were often found in that it was difficult to produce an increase in weight in some children who were much underweight because of individual peculiarities of constitution. It was seen many times that large children showed a smaller increase in weight than smaller children, which is to be related to a difference in constitution.

EMERSON, Boston.

IS SILOMILK EQUIVALENT TO CERTIFIED MILK? E. EDELSTEIN, Ztschr. f. Kinderh. **51**:650, 1931.

As a food for babies, one can expect no more and no less from Silomilk than from certified milk.

EMERSON, Boston.

PART MILK AND MILK-FREE DIETS AND THE USE OF EGGS IN INFANT FEEDING. CENEK SAITZ, Časop. lék česk. **68**:1759 (Dec. 20); 1796 (Dec. 27) 1929.

The author discusses the various indications for the use of a diet with a low milk protein content and milk-free foods, and reviews the recent literature on the various types of feeding. Almond milk, puddings of various meals (cereal), egg yolk and white, meat and vegetable soups and mayonnaise are taken up in detail. The question of true or congenital idiosyncrasy and acquired anaphylaxis is discussed. Case reports showing the use of various combinations of low or no milk protein content are given. In conclusion the author regards egg as an artificial food for the infant in spite of its manifold usefulness in various formulas. Breast milk is considered the best and only natural feeding, with which no other type can compare.

STULIK, Chicago.

CONCENTRATED SUGAR SOLUTION IN THE TREATMENT OF DEHYDRATED INFANTS. P. FLESCH, Orvosi hetil. **75**:181 (Feb. 21) 1931.

Small amounts of whey, given ten times a day together with 15 per cent maltose and a generous amount of water, had a good effect on gastro-intestinal infections in infants. This was an exclusive diet for from three to five days. The toxicity decreased, and the temperature returned to normal. Vomiting ceased, and the stools also showed improvement. It seems that a concentrated sugar solution is a reliable form of treatment in some cases of intoxication accompanying infectious diarrheas.

ZENTAY, St. Louis.

ANTIRACHITIC EFFECT OF COD LIVER OIL IN POWDER FORM. G. MANSFELD and Z. HORN, Orvosi hetil. **75**:642 (June 20) 1931.

A proprietary preparation, manufactured by the Wander Company and containing 30 per cent cod liver oil in hydrogenized form, was used in animal experimentation. The experiments were performed on rats. The animals gained in weight when the preparation was added to their diet. Rickets produced by McCollum's diet was cured if the amount of the cod liver oil preparation in the daily diet reached 1 per cent. The same concentration in the diet prevented rickets.

ZENTAY, St. Louis.

CAUSES OF HEMORRHAGES INTO THE TISSUES IN INFLAMMATORY PROCESSES (SCARLET FEVER, RHEUMATISM, ETC.). J. KON and N. ZANSMER, Pediat. polska **10**:45 (Jan.-Feb.) 1930.

The authors discuss the causes and reasons of hemorrhages into the tissues. They report a case in which they attribute hemorrhage to avitaminosis. The patient was given lemon juice, which led to an excess of vitamin C.

KUPINSKI, Chicago.

CLINICAL SIGNIFICANCE OF CRANIOTABES. I. JUNDELL, Acta pædiat. **12**:1, 1931.

Elsässer, who first described craniotabes in 1843, regarded it as a manifestation of infantile rickets. In 1908 Wieland differentiated between rachitic craniotabes and so-called physiologic craniotabes, a softening of the cranial bones along their suture margins. The latter form occurred in persons who showed no other sign of rickets, and was not influenced by antirachitic treatment. This differentiation has not been universally accepted, in spite of the support of numerous subsequent investigators. The author subjected 129 infants to intensive antirachitic therapy, which began in the prenatal period by the administration of cod liver oil or viosterol to the mother and which continued with similar treatment of the infant throughout the first two years of life. There were 79 control patients. All the patients were treated at home, except during a brief postnatal period. Softening of the cranial bones at their margins occurred fully as often among the treated patients as among the controls. The frequency was about 25 per cent in the controls, 31 per cent in the cod liver oil group and 44 per cent in the viosterol group. Softening of the centers of the bones, true craniotabes, occurred at some time in 69 per cent of the patients treated with cod liver oil, in 59 per cent of those treated with viosterol and in 58 per cent of the controls. It was noteworthy that the peak of the frequency curve of supra-occipital craniotabes was reached at about the third month in both the cod liver oil and the viosterol groups, and in the controls at about the end of the fifth month. In general, the patients showing craniotabes did not exhibit other signs of rickets any more often than those who were free from craniotabes. The author concludes that in the majority of cases craniotabes should be considered not as a rachitic phenomenon but rather as a physiologic hypoplasia.

MCINTOSH, New York.

Prenatal Conditions

CONGENITAL ESOPHAGEAL ATRESIA. EDWARD C. VOGT, Am. J. Roentgenol. **22**: 463 (Nov.) 1929.

Atresia of the esophagus is classified as follows: (1) complete absence of the esophagus (rare), (2) upper and lower segments ending in a blind pouch and (3) fistulas communicating between the upper, lower or both segments and the trachea or bronchi. Petersen reported successful esophagoplasty in a girl aged 17 years by the transplantation of a loop of small bowel. Roentgen examination is necessary in the diagnosis and differentiation in order to make the operation of any value. In the six cases reported, two patients lived for ten days, and the average length of life was seven days. Autopsy revealed an additional congenital stenosis of both ureters in one case. The immediate causes of death were pneumonia, dehydration and inanition.

STULIK, Chicago.

RIGHT UNILATERAL FUSED PELVIC KIDNEY COMPLICATING A CHRONIC APPENDICITIS. FRANCIS W. CURRIN, Am. J. Roentgenol. **22**:468 (Nov.) 1929.

A right unilateral fused pelvic kidney was demonstrated in a woman who was later operated on for chronic appendicitis, as the pain was of only a year and a half's duration and the renal anomaly was congenital.

STULIK, Chicago.

SUPERNUMERARY DISTAL PHALANX OF THE THUMB: CASE REPORT. S. M. WEINGROW, Am. J. Roentgenol. **23**:206 (Feb.) 1930.

A supernumerary distal phalanx of the thumb is described. A triple distal interphalangeal, partially functioning articulation was shown in this anomaly. A solid glans penis with an artificial meatus, made soon after birth by operation, was found in the same patient.

STULIK, Chicago.

CONGENITAL ATRESIA OF THE ESOPHAGUS WITH TRACHEO-ESOPHAGEAL FISTULA. ALEXANDER H. ROSENTHAL, Arch. Path. **12**:756 (Nov.) 1931.

Including the author's 8 cases, 255 cases of congenital esophageal stricture have been reported. In 205 of these a tracheo-esophageal fistula was also present. Clinically these infants are well developed at birth. When an attempt is made to feed them they take a few swallows readily, but then they cease to breathe, become cyanotic and regurgitate a frothy discharge through the nose and mouth. After appearing almost lifeless for a short time, they recover, to go through the same performance again if another attempt is made to feed them. If a catheter is passed into the esophagus, it meets an obstruction about 10 cm. from the alveolar ridge. The author describes the gross anatomic structure in 8 cases and the microscopic structure in 4 of these. He also discusses the various theories that have been advanced to explain the anomaly, and discards all except one presented by George L. Streeter, namely, that of an early fundamental deficiency in the entodermal cells which give rise to the esophagus. The article is well illustrated.

LESLIE, Evanston, Ill.

AN ANOMALY OF THE UMBILICAL CORD. F. F. ABBOTT, California & West. Med. **35**:126 (Aug.) 1931.

A case is reported in which the arteries of the umbilical cord made festoons of long loops from 1 to 3 inches (2.5 to 7.6 cm.) in length. One of the loops had been torn, probably by the toe of the baby, with the result that the fetus had bled to death, probably three days before labor began. Wharton's jelly was very scanty, the probable reason for the anomalous course of the blood vessels.

DICKEY, San Francisco.

THREE CASES OF PATENT DUCTUS ARTERIOSUS. JAMES E. TALLEY and MARY H. EASBY, M. Clin. North America **15**:315 (Sept.) 1931.

Three cases of patent ductus arteriosus are discussed that presented the usual clinical picture of this condition: a continuous machinery-like murmur, accompanied by a thrill in the pulmonary area; dilatation or abnormal pulsation of the pulmonary artery, and, in the two uncomplicated cases, some right-sided enlargement of the heart. In one case with superimposed rheumatic infection, the enlargement was more to the left side. Cyanosis was transient or entirely absent, and the two patients without complications led normally active lives. The electrocardiograms differed somewhat from the classic normal for this condition in that all showed increased amplitude of leads and a marked degree of left preponderance.

SMITH, Ogden, Utah.

FETAL PERITONITIS. ISAAC A. ABT, M. Clin. North America **15**:611 (Nov.) 1931.

The causes of fetal peritonitis are varied, and considerable difficulty may be experienced in determining the primary factor. Some cases are possibly due to blood-borne infections, since the transmission of certain bacteria from mother to fetus is known to occur. In the greater number of cases it follows contamination of the peritoneal cavity by the intestinal contents. This may result from per-

forations that are so minute as to escape detection or that may have become closed before the time of examination. Large rents of the intestine involving considerable of the circumference of the bowel have also been found. Since peristalsis is not thought to occur during the first half of fetal life, infections from perforations occurring during this period are likely to remain localized. Associated with perforations such malformations as atresias, bands and adhesions are commonly found. These may bear a causal relationship to the perforation or, on the other hand, may be the result of the irritative process in the peritoneum. A number of well authenticated cases of fetal peritonitis due to antenatal appendicitis have been reported. The symptoms are distention, toxemia, vomiting, dyspnea and cyanosis. Icterus is almost invariably present in those infants who are born alive.

SMITH, Ogden, Utah.

DUODENAL ATRESIA. F. BATINI, Pathologica **23**:232, 1931.

In an instance of congenital duodenal atresia, a discontinuity of the mucous membrane alone was the cause.

E. HAAM. [ARCH. PATH.]

DOUBLE URETERS. R. ERCOLE, Rev. de especialid. **6**:490 (July) 1931.

Three cases of bilateral double ureter are reported, with roentgenograms. The cases are of importance only from the standpoint of infection or resulting nephrosis. The patients were 7, 26 and 29 years old, respectively. All the patients had some pain and a turbid urine, with pus. The condition was discovered by cystoscopy and roentgenography.

SANFORD, Chicago.

THE CONNECTIONS BETWEEN THE QUANTITY OF IRON IN THE HUMAN PLACENTA AND THE DEVELOPMENT OF THE FETUS. F. C. HILGENBERG, Ztschr. f. Geburtsh. u. Gynäk. **98**:291, 1930.

The author determined the quantity of iron in thirty-five human placentas in different months of pregnancy. In males the iron content of the placenta on an average was a little lower (2.3 mg. per hundred cubic centimeters) than in females (2.48 mg.). In the placentas of children of normal weight the iron content on an average was 2.63 mg. The placentas of premature and of postmature children showed a low quantity of iron. Therefore, the iron content of the placenta increases as pregnancy advances. The author believes that the reason for this is an increased destruction of blood in the mother.

ADAIR, Chicago.

THE TRANSFERENCE OF "H" AND "O" TYPHOID AGGLUTININS FROM MOTHER TO CHILD. W. A. TIMMERMAN, Ztschr. f. Immunitätsforsch. u. exper. Therap. **70**:388, 1931.

The H and O typhoid agglutinins pass unequally through the placenta. The H form passes in most cases and the O form passes seldom if at all. Both forms are found in colostrum, in even greater concentration than in the mother's blood. The O form is more concentrated in colostrum than the H form. After ten days of lactation both forms have disappeared from the milk. The placental passage and the occurrence of the agglutinins in colostrum indicate that elective functions of living cells play a rôle in both processes.

KUGELMASS, New York.

REDUPLICATION OF THE ILEUM (ILEUM DUPLEX). F. BARTAK and J. DIVIŠ, Časop. lék. česk. **68**:1785 (Dec. 27) 1929.

A case of reduplication of the ileum with no point of communication with the regular bowel is reported. The anteoperative diagnosis at the fourth month of

life was abdominal tumor, possibly of renal origin. At operation 58 cm. of bowel was removed. This was histologically small bowel structure with an atrophic serosa. This formation could not be explained on the basis of epithelial atresia, an atypical diverticulum, an anomaly of the urorectal septum, persistent ductus omphalomesentericus or any other previously described anomaly. The explanation must be sought in the development of the bowel at the time of closure of the primary intestinal groove, at which time a separate loop of bowel may have been pinched off.

STULIK, Chicago.

Diseases of the New-Born

UNFOUNDED DIAGNOSES IN NEW-BORN INFANTS THAT DO NOT SURVIVE. JOHN W. WILLIAMS, M. J. & Rec. **134**:493 (Nov. 18) 1931.

Many inaccurate diagnoses of the cause of death in new-born infants are given by physicians. Often they realize that these diagnoses are incorrect, but they are unable to give more accurate ones. One great reason for this lack of ability is the lack of money for research in this field. Billions are spent for research in cancer in trying to determine its cause and cure, but there is no money to clear up this chaos relating to the advent of a new existence. True, the glory of the discovery of the cause and the cure of cancer will be great, but the reward of seeing the little fellow who would otherwise be lost grow strong and healthy will yield greater satisfaction.

WILLIAMSON, New Orleans.

VARIX OF THE UMBILICAL CORD, WITH CASE REPORT. ROBERT E. MCDONALD, Wisconsin M. J. **30**:642 (Aug.) 1931.

Reports of varix of the cord have been infrequent. Most of the babies presenting this difficulty have been stillborn owing to rupture of the varix with resulting exsanguination. Some die of clot formation and the blocking of arterial flow from the mother rather than of rupture. The case reported is of the latter type, and the infant lived. It was the mother's third breech presentation (corrected by external version). The pregnancy was full term, and rapid delivery was effected with forceps after nine hours' labor and after the fetal heart rate had gone up to 166. The infant was in a condition of asphyxia pallida. There was a tumor, dark reddish-blue and the size of a walnut, close to the junction of the skin with the cord. The tumor contained a clot not more than a few hours old and nearly occluding the lumen of the dilated vein. Resuscitation was accomplished after twenty minutes.

JANNEY, Milwaukee.

DISCUSSION ON INTRACRANIAL INJURY IN THE NEWLY BORN AND ITS RELATIONSHIP TO BREECH DELIVERY. J. R. CAMERON, Tr. Edinburgh Obst. Soc., 1930-1931, p. 137; in Edinburgh M. J., October, 1931.

Cameron saw intracranial hemorrhage of the newly born in six cases of primary breech presentation, one complicated by a contracted pelvis. At a meeting of the Obstetrical Society he presented some actual specimens showing the damage done to the tentorium and falx. There is a great danger of laceration of the dural septums with hemorrhage when the head is not sufficiently flexed while it passes the pelvic brim if the measurements are disproportionate, or in extraction if the head is too rapidly compressed. In premature infants the dura is not mature and is more susceptible to injury. Even cases of normal spontaneous breech delivery may show intracranial injury and hemorrhage.

At autopsy Cameron used the excellent technic of Beneke in opening the skull and examining the contents. He found four types of tears in the six cases: a superficial unilateral tear of the tentorium, a complete tear of both superficial vertical and deep horizontal fibers of the tentorium, bilateral tears of the tentorium

and laceration of the falx involving also the tentorium. There was subdural intracranial hemorrhage in all cases. Clots were demonstrated above, below and between the layers of the tentorium. If any hemorrhages occurred in the brain they were microscopic. Ventricular hemorrhage was not present. The mechanism of delivery of the head in each case is mentioned. Within six months at the hospital there were seventy-seven breech deliveries, among them forty-five cases of complicated breech presentations and eight deaths. Intracranial hemorrhage and tears were present in 11 per cent of these forty-five cases. In fatal cases, death was due to laceration of the tentorium and hemorrhage in from 62 to 82 per cent. Treatment was based on the trauma or on a hemorrhagic diathesis. The head was kept raised, and magnesium sulphate in a 50 per cent solution was given in one-half drachm (1.9 Gm.) doses for cerebral edema. The child was not moved unnecessarily. Lumbar puncture was tried in some cases.

Dr. Cameron, in closing the discussion, stated that at operation on the skull for epileptic seizures he had seen two instances of gross scarring of the brain. One was in an adult with a history of birth by breech delivery. Some of the openings seen in the falx at autopsy are normal aperturae and not due to trauma. Professor Johnstone, in discussion, said that breech presentations should, if possible, be avoided in primiparae, or the head should be delivered slowly, with less likelihood of a tear. The head could probably remain in the pelvis longer than is usually permitted.

NEFF, Kansas City, Mo.

HEMORRHAGE INTO THE VENTRICLES. GAUTRET and REUON, Nourrisson **19**: 284 (Sept.) 1931.

The case reported is of interest because the signs of hemorrhage appeared late. The baby was born at term of a quadriparous mother and weighed 2,540 Gm. The labor was short and natural. The infant progressed normally for a week and then showed signs of intracranial disease. The cerebrospinal fluid obtained by lumbar puncture contained red blood cells. Autopsy confirmed the diagnosis of ventricular hemorrhage.

MCCLELLAND, Cleveland.

FATAL STREPTOCOCCUS INFECTION IN A MOTHER AND CHILD. M. A. FRUHINSHOLZ, Nourrisson **19**:286 (Sept.) 1931.

On the eleventh day post partum the mother had a fissure in the right nipple with signs of lymphangitis. The baby was continued on the breast; it soon showed vomiting and diarrhea, and several successive areas of dermatitis appeared on the forehead, neck, back and buttocks. Small doses of antistreptococcus serum were unavailing; death followed in a few days. The infection persisted in the mother and extended to the right axilla, arm and back; the left breast was also involved. Injections of serum and transfusions were given without benefit. Blood cultures gave negative results. Death occurred on the thirty-sixth day.

MCCLELLAND, Cleveland.

GASTRO-INTESTINAL HEMORRHAGE IN THE NEW-BORN. VORON and E. BANSSILLON, Nourrisson **19**:290 (Sept.) 1931.

A full term baby had hematemesis twenty hours after birth. Melena followed. Treatment by mouth with gelatin water and epinephrine was unsuccessful in controlling the hemorrhage. On the fourth day a transfusion with citrated blood was given into the fontanel; the baby died twenty-six hours later. Postmortem examination showed a marked congestion of the mucosa of the stomach and duodenum without ulceration. An extradural hematoma at the site of the sinus puncture was also found. The gastro-intestinal hemorrhage was thought to be the cause of death.

MCCLELLAND, Cleveland.

THE CLINICAL RÔLE OF THE PHYSIOLOGY AND PATHOLOGY OF THE NEW-BORN. M. ERLICH, Rev. franç. de pédiat. **7**:669 (Oct.) 1931.

The author pleads for more space in the curriculum for the study of the new-born. Its importance is shown by the placing of such study in a prominent position at the recent International Congress of Pediatrics at the Hague.

SANFORD, Chicago.

BACILLUS COLI AGGLUTININS IN THE NEW-BORN AND OLDER INFANTS. EGLE INGLESSI, Riv. di clin. pediat. **29**:715 (Sept. 15) 1931.

In the blood of thirty-five infants under 4 months of age no agglutinins of Bacillus coli were found. Beginning at the fourth month of age, agglutinins were found in increasing number until the sixteenth month, when the blood reached the titer of adult blood. The blood of the mothers of some of the new-born infants was studied, and in each case agglutinins were found. No agglutinins were found in the blood of the placenta or the umbilical cord.

HIGGINS, Boston.

EXFOLIATIVE DERMATITIS IN A NEW-BORN INFANT. M. PACHECO, Rev. de especialid. **6**:913 (Oct.) 1931.

A generalized vesicular eruption developed which caused considerable exfoliation, enough to class it as Ritter's disease. Recovery occurred in about two weeks. During the exfoliative period potassium permanganate baths were given.

SANFORD, Chicago.

THE BLOOD SUGAR DURING THE FIRST DAYS OF LIFE. G. SCHRETTER and H. NEVINNY, Ztschr. f. Geburtsh. u. Gynäk. **98**:258, 1930.

The authors examined the blood sugar of 38 new-born infants in the fasting state during the first week of life. Frequently they found surprisingly low values. Ninety-five of the 196 single values were under 0.07 Gm. per hundred cubic centimeters, and 15 were so low that if the subjects had been adults there would have been signs of hypoglycemia. High values were rare. The variations in each case were remarkable.

In the beginning one sees the lowest values and later a gradual increase. At the end of the first week of life, the normal value of the blood sugar of the adult is usually reached.

The authors interpret these findings as the result of the change of food after birth, the change of the regulation of body temperature, the endocrine system of the new-born, etc.

ADAIR, Chicago.

THE INDICAN CONTENT IN THE SERUM OF MOTHER AND CHILD AT THE END OF NORMAL PREGNANCY. SIEGFRIED HENSEL, Ztschr. f. Geburtsh. u. Gynäk. **98**:276, 1930.

The author determined the indican content in the serum of thirty pregnant women and their offspring and that of ten nonpregnant women. The conclusions drawn from his investigations were as follows:

The indican content of the blood in pregnant women at term is not higher than that of nonpregnant women. The author could not verify the findings of other research workers who found a "physiologic hyperindicanemia during pregnancy." The blood of the fetus contains more indican than that of the mother. This substance does not appear in the urine of the new-born until some hours after birth.

The author believes that the cause of the augmentation of indican in the fetus is the increase in intermediate metabolism of albumin.

ADAIR, Chicago.

ORIGIN OF INTRACRANIAL HEMORRHAGE IN THE NEW-BORN. J. K. KUHN, Ztschr. f. Geburtsh. u. Gynäk. **99**:297, 1931.

Most authors think that violence to the skull is the cause of intracranial hemorrhage in the new-born (Beneke, Benthin, A. Mayer). A second group of writers believes that asphyxia of the new-born is the cause, or at least an important preliminary condition, of hemorrhage (L. Seitz). Schwartz is of the opinion that the change in pressure which takes place in the part of the skull below the os uteri after the rupture of the amniotic sac is the cause of rupture of vessels in the region of the vena magna galeni. This rupture is the cause of hemorrhage.

The author dissected fifty-six children who died during or soon after birth. In eighteen he found fatal intracranial hemorrhage. Fourteen of these showed a rupture of the tentorium and other hemorrhages. Seven cases of rupture of the tentorium took place soon after spontaneous delivery; six of the mothers were primiparae. In four cases the pelvis was contracted. Eight cases were operative deliveries: four versions and extractions, one external version, two forceps deliveries and one section.

From his observations the author believes that traumas of the skull of the child are the main cause of intracranial hemorrhage, and that less pressure is not of great importance.

It is his opinion that in spontaneous deliveries the lateral or longitudinal disarrangement of the bones of the skull is the cause of hemorrhage. The location of the hemorrhage could be predicted in most cases from the type of molding of the skull and the position of the caput succedaneum.

ADAIR, Chicago.

CHRONIC GENITAL EDEMA OF THE NEW-BORN. J. BRDLIK and J. SVEJCAR, Časop. lék. česk. **68**:1717 (Dec. 13) 1929.

A review of the literature is followed by a classification of the etiologic factors into: (1) mechanical causes, such as pressure of intra-uterine or extra-uterine type; (2) humoral causes, such as the reaction of pregnancy; (3) infections, and (4) sensitivity of the capillaries of the new-born. In the six reported cases, one patient had an associated naval granuloma, one pemphigus, one periumbilical deep infection, one septicemia and two congenital syphilis. In the syphilitic infant autopsy did not reveal a reason for the location and intensity of the edema. Most authors are tempted to explain the edema on the basis of a poorly developed intima and a well developed elastic layer. The localization in the genital region may be due to progression from a periumbilical or deep abdominal infection. The possibility of congenital syphilis must not be overlooked.

STULIK, Chicago.

Acute Infections

THE PATHOGENESIS OF ACUTE SUPPURATIVE PAROTITIS: AN EXPERIMENTAL STUDY. A. L. BERNDT, R. BUCK and R. VON L. BUXTON (under the Direction of R. P. Custer), Am. J. M. Sc. **182**:639 (Nov.) 1931.

Dogs were used throughout the entire experiment. Hemolytic Staphylococcus aureus bouillon cultures of both high and low virulence were used. In two instances a mixed culture of staphylococci and pneumococci from a person with acute suppurative parotitis was used. The work was done in an attempt to produce an inflammatory response by two methods, either confirming or discrediting Rost's work done in 1914. It was found that acute suppurative parotitis can be produced by either means of injection, but is produced with greater facility through the duct. The histopathologic picture in the two instances is not identical, which is the reverse of Rost's statement.

HENSKE, Omaha.

A Survey of Diphtheria Prevention in Philadelphia. Edward L. Bauer, Am. J. M. Sc. **182**:839 (Dec.) 1931.

Approximately 55 per cent of the children of preschool age in Philadelphia have been immunized against diphtheria. Of the children of preschool age receiving no immunization doses, approximately 25 per cent are naturally immune, bringing the grand total of the infant and preschool age population of Philadelphia who are immune to diphtheria to about 66 per cent. The incidence of diphtheria has been reduced 80 per cent. Ninety-nine and two-tenths per cent of cases occurring in the city of Philadelphia are seen in nonimmunized children or in those in whom no immunity has been demonstrated. Bacteriologically, the disease retains its usual degree of virulence, and the death rate continues as high as ever. Considering all other factors, active immunization seems to be the means of combating and eradicating diphtheria. Complete explanatory tables and charts accompany the article.

Henske, Omaha.

Treatment of Whooping Cough with Convalescent Serum. J. C. S. Battley, Arch. Pediat. **48**:675 (Oct.) 1931.

Two cases of whooping cough are reported; one patient was treated with convalescent serum, and the other with convalescent whole blood. Improvement appeared to follow this method of therapy. The author cites previous reports of apparent good results from convalescent serum and injections of whole blood.

Waddell, University, Va.

An Unusual Case of Varicella. Alfred V. Salomon, Arch. Pediat. **48**: 679 (Oct.) 1931.

A case of varicella complicated by a streptococcus infection of the throat, bilateral mastoiditis, sinus thrombosis and bacteremia is reported. An interesting point is presented in the following questions: "First, whether this child, through its exposure to a known scarlet fever case, actually contracted a scarlet fever infection without the usual cutaneous manifestations, which was brought under immediate control by the rapid and intensive use of scarlet fever antitoxin, and second, whether the virus or secondary invading organisms of the original varicella lesion had spread and caused their most serious damage at the point of original irritation, the nasopharynx and the internal ear. The latter point which bears out the contention of Rivers concerning the elective localization of varicella lesions at points of pre-existing irritation has much to commend it."

Waddell, University, Va.

Notes of New Cases of B. Dysenteriae Sonne Infection. Marion W. Johnston and Alan Brown, Canad. M. A. J. **25**:417 (Oct.) 1931.

The authors present a summary of sixty-eight cases of infants sent to the Hospital for Sick Children at Toronto. Fifty-three of these were diagnosed as acute intestinal intoxication, and the remainder were diagnosed as infectious diarrhea, fermental diarrhea and dysentery. Eleven strains of Bacterium dysenteriae Sonne were isolated from these cases. The conclusions from the study were that Bact. dysenteriae Sonne appears to be the etiologic factor in gastro-intestinal disturbances during the season of epidemic diarrhea as well as during the colder months of the year. Infections were especially numerous and serious among children under 2 years of age.

Moore, Omaha.

The Immunization of the Pre-School Child Against Diphtheria by the Use of Toxoid. A. B. Schwartz and F. R. Janney, Wisconsin M. J. **30**: 719 (Sept.) 1931.

The value of preventive immunization against diphtheria is shown by a comparison of the incidence and mortality rates for unprotected children with those for

children who have been immunized. The Schick test should always be done to determine whether or not immunization has been complete. Otherwise, from 1 to 20 per cent are not sufficiently protected; in some of them diphtheria may later develop, and the whole procedure may thus be discredited. In approximately 80 per cent of those given toxin-antitoxin a negative Schick reaction develops, while from 95 to 100 per cent of those given the three dose toxoid preparation are protected. Immunization should be done early (from the sixth to the twelfth month), since diphtheria is most serious during the preschool age. Of 200 children, aged from 6 months to 6 years, given toxoid, 199 subsequently showed negative Schick reactions. Reactions were slight, particularly in the younger children.

JANNEY, Milwaukee.

THE TECHNIQUE OF DETECTING DIPHTHERIA BACILLUS CARRIERS AND ITS APPLICATION. R. A. Q. O'MEARA, J. Hyg. **31**:473 (Oct.) 1931.

Detection and isolation of virulent diphtheria carriers comprise one of the methods of preventing diphtheria and are especially important in schools for young children where a large proportion are susceptible. Their detection has not been very successful, and methods of procedure up to the present are vague. An elaborate but highly efficient technic for the determination of virulent carriers is given in detail. Nasal carriers are as frequent as throat carriers. Carriers of virulent and nonvirulent organisms are distinguished by animal inoculation after a series of cultures on special mediums are made from the original swab.

JANNEY, Milwaukee.

THE OCCURRENCE OF SCARLATINAL TYPES OF STREPTOCOCCI IN NON-SCARLATINAL INFECTIONS. V. D. ALLISON, Lancet **2**: 844 (Oct. 17) 1931.

After studying the strains of hemolytic streptococci isolated from 400 patients suffering from scarlet fever, the author studied in a similar manner strains of hemolytic streptococci from patients with infections other than scarlet fever. Only 8 of the latter group (a total of 396 strains) were found to belong to one or another of the 4 main serologic types of scarlatinal streptococci. Among the 8 typed strains, a type I strain and a type III strain were isolated from uterine cervical swabs in cases of puerperal infection, while a type I strain and a type III strain were isolated from the throat swabs of midwives in attendance in the respective cases.

LANGMANN, New York.

DIRECT LARYNGOSCOPY AND ASPIRATION IN LARYNGEAL DIPHTHERIA. W. T. BENSON, Lancet **2**:956 (Oct. 31) 1931.

The author makes a strong plea for the use of the laryngoscope, especially in cases in which symptoms of croup are suspected of being due to diphtheritic infection. Its use will indicate the best method of relieving the respiratory distress. Aspiration is indicated when dyspnea is due to extensive membrane formation. When gross subglottic edema is the cause of the respiratory difficulty, operative measures are necessary.

LANGMANN, New York.

PARALYSIS OF THE BRACHIAL PLEXUS FOLLOWING SERUM THERAPY FOR DIPHTHERIA. H. ROGER, C. MATTEI and J. PAILLAS, Ann. de méd. **29**:610 (May) 1931.

Nine cases of paralysis of the arms, including three cases personally observed, following injections of diphtheria antiserum were analyzed. All the reports were published in the French literature. Adults (from 16 to 34 years) only were affected. Following the injection of an average dose of from 20 to 60 cc. of antiserum, generalized urticaria, edema of the legs and fever and pain, arthritic in type, developed.

The pain receded and was finally localized in the upper part of the shoulder. A flaccid paralysis of the shoulder and the upper part of the arm followed, with a diminished reaction of the muscles to electric stimulation and sometimes the complete reaction of degeneration. Next, muscular atrophy was noticed and persisted for a long time, even after the regaining of function. Disturbances of sensation were usually added to the picture of motor paralysis; there were complaints of burning, lancinating pains or simple paresthesias. Objectively a mild hyperthesia, with a transition to anesthesia, was found with a predilection for the area of the cutaneous branch of the circumflex nerve. Motor and sensory disturbances remained stationary for many months, and complete recovery occurred very slowly.

There can be no doubt that this type of paralysis is not produced by the diphtheria toxin directly. Sicard and de Gennes considered it as an allergic phenomenon, and thought that urticaria and edema produced this lesion of the more sensitive nerves of the brachial plexus. Other authors assumed a lesion in the spinal cord. Lhermitte was in favor of a radicular origin; others considered it a peripheral lesion. Such accidents may be prevented by the use of purified and albumin-free antiserums, preceded by injections of carbonates or citrates. The treatment consisted of electrical stimulation in connection with strychnine.

WEIL, Chicago. [ARCH. NEUROL. & PSYCHIAT.]

ABORTIVE SCARLATINA OF THE PRURIGINOUS TYPE. P. HÉRITER, Arch. de méd. d. enf. **34**:553 (Sept.) 1931.

Among the rarer types of scarlet fever is that associated with prurigo. Rilliet and Barthez in their authoritative contribution could not report a single instance, although they mentioned the fact that during the stage of onset in many cases of scarlatina the itching is intolerable. Hériter describes a case in a girl, aged 4 years, following a burn of the second degree; the site was not stated. The onset was brusque, with a high temperature (104 F.) and a pulse rate rising rapidly to 160; pruritus was intense, but vomiting was restricted to one attack. The case proceeded like one of almost malignant type, but the dominating symptom throughout was the uncontrollable itching. The importance of the differential diagnosis is suitably emphasized.

AMESSE, Denver.

MEDICOSURGICAL STUDIES OF PERFORATIONS OF THE GALLBLADDER IN THE COURSE OF TYPHOID FEVER. R. LIÉGE and A. FOLLIASSON, Arch. de méd. d. enf. **34**:581 (Oct.) 1931.

A case of typhoid fever with perforation of the gallbladder in a boy, aged 11 years, is reported in full; cholecystostomy was performed, and after a critical period the child recovered. The study of this invasion stimulated the authors to review the literature of biliary complications in the course of enteric fever, and especially the relative values of cholecystostomy and cholecystectomy in the management of perforation. In a discussion of acute cholecystitis as a complication of typhoid, Reid and Montgomery reported eighteen such cases published between 1835 and 1919, ten of which resulted in perforation. Ritter and Ehrat found eleven additional cases in the literature between 1919 and 1928, without stating the number in which perforation was observed, but it is asserted that the percentage is high, amounting to 46 per cent of the total series of thirty-five authentic cases reported. Following a brief period of involvement with pain in the upper right quadrant, perforation is prone to occur between the second and the fourth week of typhoid fever; it stimulates perforation of the intestine in that region so perfectly that the differential diagnosis is extremely difficult. In either instance the obvious treatment is surgical intervention followed by supportive measures judiciously outlined. Liége and Folliasson stress the value of drainage in every severe case of cholecystitis so as to prevent rupture and the resulting peritonitis.

AMESSE, Denver.

MATERNAL BLOOD AS A PROPHYLACTIC. P. JOANNON, Progrès méd., December, 1931, p. 2301.

The author discusses the factors involved in maternal measles and the immunity conferred. If the mother has had measles before gestation, injection of her blood into the child is useless before the latter is 6 months of age. From 6 months to 2 years of age it is indicated. After 2 years it may not be effective.

SANFORD, Chicago.

AN EPIDEMIC DISEASE IN INFANTS CHARACTERIZED BY A MILIARY EXANTHEM. A. STROÉ, Rev. franç. de pédiat. **7**:467, 1931.

The author describes a disease that was epidemic in infants' hospitals in Bucharest in 1923, the symptoms of which do not fall into any of the accepted classes of exanthems. The incubation period was from six to fourteen days. The period of invasion was two to five days. This was characterized by a temperature of from 38 to 39 C (100.4 to 102.2 F.), an oculonasal catarrh and a redness of the tonsillar pillars. The exanthem consisted of small, rose red macules which tended to form plaques and on which small vesicles formed as a final stage. These either were absorbed or ruptured, causing a desquamation. The desquamation was present on the face, body, extremities, palms and soles. The disease was contagious for two thirds of the children exposed. The blood showed a mononucleosis of 70 per cent, and there was sometimes an apparent increase of cerebral pressure. One case was considerably relieved by a spinal puncture. The spinal fluid was normal.

SANFORD, Chicago.

MALARIA AND THE CHILD. C. J. KRUIMEL and D. J. E. SIGAL, Rev. internat. de l'enf. **12**:3 (July-Aug.) 1931.

At the recent International Congress for African Children, held in Geneva, several important contributions were made on paludism and its effects on the growing child. The present paper comes from the Bureau for the Encouragement of the Use of Quinine, Amsterdam, and is an exhaustive monograph divided into four sections. The first is concerned with the influence of malaria on pregnancy. The authors assert that it may affect the birth rate in several ways: It impedes reproduction, it is a frequent source of abortion and it has a deleterious action on the new-born infant. In the French Colony of Maroni, 215 of 418 marriages registered in twenty-three years were entirely without issue, while of 370 children born alive, 238 died in early infancy. Observers are not in accord concerning the question of congenital malaria. In Dalmatia intensive studies have been made by Weselko, who believes the theory entirely tenable but the actual route of infection not clearly understood. Medical experience opposes the view that therapeutic doses of quinine during pregnancy are harmful; this drug is even more essential for pregnant than for nonpregnant women. Investigations at the Maternity Hospital of Dakar, however, have led to the conclusion that quinine is not secreted in sufficient amount in the milk of nursing mothers to protect the infant. The second topic of the article embraces the clinical study of malaria in the infant and the growing child. In addition to the well known symptomatology, attention is called to the unusually severe involvement of the spleen, with resulting hypertrophy, great deformity and the constant menace of fatal hemorrhage from falls or blows. After the tenth or twelfth years there seems to be a considerable degree of immunity in African children, unlike the observations in Java, China and India. A third section is devoted to statistics on malaria in children, which shows the appalling loss of life from this preventable disease in backward countries, and the fourth discusses those methods of prophylaxis and treatment which have been universally adopted. A particularly valuable bibliography accompanies the article.

AMESSE, Denver.

THE SCHICK TEST IN THE PROVINCE OF PAVIA. P. MOLTENI, Riv. di clin. pediat. **29**:803 (Sept. 15) 1931.

Schick tests were performed on 714 children between 1 month and 12 years of age. The results were positive in 41 per cent; this percentage is higher than that reported for other Italian cities. Tests were postive in 14 (27 per cent) of 52 children under 1 year of age, in 66 (62 per cent) of 106 between 1 and 5 years old, and in 38 per cent of the older children. Of 35 susceptible children given active prophylactic treatment (anatoxin), 29 showed a negative Schick test one month later.

HIGGINS, Boston.

VACCINE TREATMENT IN WHOOPING COUGH. E. ERBEN, Med. Klin. **27**:1174 (Aug. 7) 1931.

The author reports six cases of pertussis. Four of the patients were treated with vaccine; two did not receive any treatment. Four injections of pertussin were given to each of the four children. No marked difference could be noted in the course of the disease in the two series.

ZENTAY, St. Louis.

OBSERVATIONS IN A HOUSE EPIDEMIC OF SCARLET FEVER. H. KLEINSCHMIDT, Med. Klin. **27**:1409 (Sept. 25) 1931.

The report deals with a house epidemic during which fourteen cases were seen in the course of five months. The infections occurred mostly among the personnel. The origin of the epidemic seemed to be obscure. No carrier of Mandelbaum's bacillus was discovered. Besides typical forms of scarlet fever, many cases of tonsillitis were observed. Some of these cases showed desquamation and changes on the finger nails, and possibly should be classified as abortive forms of scarlet fever. Children under 1 year of age, in spite of definite exposure, did not contract the infection. The absence of hemolytic streptococci in the first smear does not rule out scarlet fever. Passive immunization with scarlet fever antitoxin, in spite of the rather high dosage of 5 cc. of concentrated serum, failed twice in seven cases. This failure of antitoxin in the toxic forms of scarlet fever did not coincide with previous observations. It seems that the therapeutic action of scarlet fever serum cannot be explained on the same basis as the action of other antitoxic serums. Active immunization with the streptococcus ointment of Löwenstein resulted in complete failure, as new cases appeared fifty-nine days after the first application.

ZENTAY, St. Louis.

DIPHTHERIA SUSCEPTIBILITY ACCORDING TO DIFFERENT BLOOD GROUPS. HERBERT NOWAK, Monatschr. f. Kinderh. **51**:257 (Nov.) 1931.

It is known that human blood can be divided into four different groups. Several observers have attempted to relate susceptibility to disease to any one of these blood groups, but without success. The author attempts the same problem with the Schick test as an index of natural susceptibility. In 384 children, he could find no special difference in the natural susceptibility of any of the blood groups. Of especial interest, however, was the observation that after having suffered from active diphtheria the children of group A showed much less immunity than the children of the other three groups. He concludes that the children of group A have less ability to build antibodies after an attack of diphtheria than the children of the other three groups.

GERSTLEY, Chicago.

OTOGENOUS MENINGITIS IN AN INFANT; RECOVERY AFTER ANTHROTOMY. G. KEREKES, Orvosi hetil. **75**:589 (June 6) 1931.

In a 14 months old infant meningitis developed during the second week of purulent otitis media. The cerebrospinal fluid was turbid and staphylococci were

obtained in culture. Retro-auricular anthrotomy was performed, and after a stormy course, the child improved. It seems that even in a fully developed case of meningitis, anthrotomy is indicated and occasionally may lead to recovery.

ZENTAY, St. Louis.

SEPTICEMIA IN AN INFANT, DUE TO MICROCOCCUS TETRAGENUS. J. KRAMAR, Orvosi hetil. **75**:713 (July 4) 1931.

Micrococcus tetragenus is usually considered as a harmless saprophyte. Occasionally it may cause localized or generalized infection. This seems to be the first case in the literature in which this organism produced a septicemia. The infant was not acutely ill, but the temperature was extremely high, ranging between 40 and 41 C. (104 and 105.8 F.). The fever lasted over ten weeks. Physical examination gave negative results. Culture of the blood gave a pure growth of Micrococcus tetragenus. The serum of the infant agglutinated this organism in the dilution 1:640. The author thinks that the peculiar clinical picture, which was different from the usual course of septicemia, can be explained by two factors: first, that the organism is of a mild and only occasional pathogenic variety; second, that the infant seemed to have had a very labile center of heat regulation that must have accounted for the high and protracted curve of temperature.

ZENTAY, St. Louis.

SCARLET FEVER: VIII. RELAPSES, THEIR NATURE AND PREVENTION. A. LICHTENSTEIN, Acta pædiat. **12**:75, 1931.

The frequency of relapse in scarlet fever has recently been on the increase in Stockholm. It was found that patients isolated in pairs throughout their entire stay in the hospital showed less than half the frequency of relapse shown by a control group kept in a general ward. Among those rigidly isolated there were no relapses, nor did any occur when two children of the same family were isolated together. In the control group, it was found that relapses spread from bed to bed in a ward, picking out as a rule patients whose reaction to the Dick test remained positive late in the course of the disease or during convalescence. Vaccinotherapy, if continued until a negative Dick reaction was obtained, appeared to protect the patient against relapse. The evidence offers strong support to the theory that relapses are due to superinfection with a second strain of scarlatinal streptococcus.

MCINTOSH, New York.

SCARLET FEVER: IX. THE EFFECT OF INDIVIDUAL ISOLATION ON THE COURSE AND COMPLICATIONS OF SCARLET FEVER. A. LICHTENSTEIN, Acta pædiat. **12**:95, 1931.

Individual isolation of scarlet fever patients, as carried out in the preceding investigation, greatly reduced the frequency of complications, particularly otitis media, mastoiditis, sinusitis and adenitis. Isolation appeared to retard the change in the Dick reaction from positive to negative. It had no effect on the incidence of hemolytic streptococci in throat cultures.

MCINTOSH, New York.

SCARLET FEVER: X. RETURN CASES. A. LICHTENSTEIN, Acta pædiat. **12**:100, 1931.

The frequency with which patients convalescent from scarlet fever infect others after their discharge from the hospital depends primarily on their clinical condition on discharge, especially on the presence of pyogenic complications. The presence or absence of hemolytic streptococci in the throat at the time of release is, with present methods, a poor guide of infectiousness and should not be relied on as an indication that the normal isolation period may be curtailed in individual cases.

A number of return cases appear to be dependent on the occurrence of relapse. Individual isolation during the course of the disease appears to have a beneficial influence on the frequency of return cases, apparently through its effect on the suppression of relapses. Recent attempts to immunize the susceptible contacts in the home before the patient's release from the hospital have appeared encouraging.

McINTOSH, New York.

Chronic Infections

THE ABSCESS OF POTT'S DISEASE. RALPH K. GHORMLEY, Am. J. Roentgenol. **22**:509 (Dec.) 1929.

The author discusses the thoracic and lumbar abscess of Pott's disease and classifies the former into the fusiform, pyramidal and globular types or a combination of these. There is a marked difference in the behavior of these abscesses because of the variations in the anatomic structure of the two regions. The thoracic abscess is a serious menace because of its influence on the deformity, but of less danger to life itself. The lumbar abscess of Pott's disease is a more serious menace to life because it may rupture through the fascia, and many patients with sinus formation die of infection or the complication of amyloid disease. A plea is made for good films so that the abscess may be diagnosed before gross changes appear and before rupture into the groin or other soft tissues.

STULIK, Chicago.

THE TUBERCULOUS PULMONARY CONSOLIDATIONS OF CHILDHOOD. GARRETT R. MILLER, M. Clin. North America **15**:449 (Sept.) 1931.

Three distinct forms of tuberculous consolidation occur in the lungs in children, representing entirely different phases of the disease. The pathogenesis of these lesions is easily understandable, yet they are sufficiently alike in their early clinical and roentgenologic appearances to cause difficulty in diagnosis. 1. The progressing or spreading primary form. The primary focus fails to heal, resulting in an extensive gelatinous consolidation, which may assume lobar proportions. The tracheobronchial lymph nodes are likely to become massively involved. Ultimately excavation occurs, tests of the sputum become positive and by aspiration further involvement of the lungs develops. The lesion is usually fatal. In rare instances healing takes place with considerable residual calcification and fibrosis. 2. Progressive consolidation of reinfection. In a previously infected and allergic child, a heavy dose of bacilli may produce a consolidation made up of a collateral inflammatory reaction and caseation necrosis. The onset is usually abrupt, and the lesion is likely to progress to cavitation with subsequent involvement of the lung elsewhere by aspiration. The condition is unstable, with periods of recrudescence and abeyance, but ultimately is usually progressive. Healing proceeds from the periphery and throughout the central portion, leaving areas of scar tissue and considerable calcification. Progressive involvement of the lungs is a common picture. 3. Benign consolidation of reinfection. The pathology of this lesion is uncertain since it is only from its roentgen characteristics that the condition is known. The most plausible explanation is that a light dose of reinfecting bacilli is distributed uniformly in a lobe or part of a lobe resulting in a collateral inflammatory reaction that makes up most of the consolidation. There is probably little caseous material in the lesion. In children, chiefly between the ages of 4 and 12 years, it appears suddenly with a slight systemic reaction and is manifest as a homogeneous density, usually in part of an upper lobe. The consolidation clears from the periphery inward in from several months to a year and, on healing, leaves slight pulmonary markings. No progressive lesions or cavitations are seen. The diagnosis is difficult and frequently impossible from a single examination. The terms epituberculosis, basal tuberculosis, etc., have been loosely applied to any and all of these consolidations.

SMITH, Ogden, Utah.

TONSILS AND ADENOIDS IN RELATION TO TUBERCULOUS INFECTION. MICHAEL ALASTO, Brit. J. Tuberc. **25**:129 (July) 1931.

Secondary infection of the tonsils in adults suffering from advanced pulmonary tuberculosis is relatively common, probably owing to contact with bacillus-laden sputum. In children the sputum is usually swallowed, and involvement of the tonsils rarely occurs. Primary tuberculosis of the tonsil is, in most cases, due to infection with the bovine bacillus, which enters the system by way of the alimentary tract. Except in rare instances, the clinical diagnosis of tuberculosis of the tonsil is impossible. The appearance of the organ is no guide whatsoever in the recognition of the condition. The presence of an enlarged gland in the area between the upper part of the sternocleidomastoid muscle and the lower jaw immediately over the posterior belly of the digastric muscle, while indistinguishable from infection by the usual pyogenic organisms, is perhaps the most suggestive sign of tuberculous infection involving the tonsil.

SMITH, Ogden, Utah.

AN INVESTIGATION INTO THE PART PLAYED BY MATERNAL SYPHILIS IN THE CAUSATION OF FETAL AND INFANT DEATH AND THE EFFECTS OF ANTENATAL TREATMENT. E. J. PYE-SMITH, J. Obst. & Gynæc. Brit. Emp. **38**: 578, 1931.

The author concludes from the careful study of his cases that maternal syphilis is not a common cause of abortion, either before or after the third month of pregnancy. It is, however, an important cause of stillbirth and of infant death from syphilis or intercurrent infections. Death is most frequent during the first six months of life. The treatment of the mother during pregnancy is of great benefit, as the percentage of premature births is reduced, the percentage of live births is raised, and proportionately more infants survive the first year of life whose mothers are treated than whose mothers are not treated. The results of the investigation indicate that the incidence of maternal syphilis in the author's locality is probably less than 2 per cent. He believes that abortion is not especially common among syphilitic women. Maternal syphilis causes the most harm in the later weeks of pregnancy and the first months of postnatal life, as stillbirths and infant deaths are much more frequent when the mother is the subject of syphilis. Good results follow treatment with neoarsphenamine, even when an efficient course cannot be given: The disease is not so common, the treatment is easily applied and it is followed by a suppression of the more disastrous consequences of the disease.

ADAIR, Chicago.

PRECOCIOUS INTERSTITIAL KERATITIS. A. IANCOU, Nourrisson **19**:278 (Sept.) 1931.

Interstitial keratitis is one of the late manifestations of congenital syphilis. That it may occur in early infancy is shown by a review of the literature. The author reports two additional cases occurring in girls aged 4 and 3½ months, respectively. In one case the keratitis developed while the baby was receiving antisyphilitic treatment with neoarsphenamine.

MCCLELLAND, Cleveland.

FREQUENCY OF TUBERCULOUS LESIONS IN CHILDREN WITH PHLYCTENULAR KERATITIS. P. WORINGER, Paris méd. **2**:398 (Nov. 7) 1931.

Of sixty-seven children with phlyctenular keratitis, fifty-seven reacted to tuberculin and ten had no reaction. By roentgenograms peribronchial adenopathy was demonstrated in a majority of cases, frequently accompanied by calcification.

SANFORD, Chicago.

THE URINARY MANIFESTATIONS OF CONGENITAL SYPHILIS IN INFANCY. F. WEISS, Rev. franç. de pédiat. **7**:482, 1931.

Renal involvement is rather common in many cases of congenital syphilis. The urine shows albumin, cellular elements, hyalin, granular casts and leukocytes. There is also a constant tendency to eliminate erythrocytes. Their appearance is almost always a sign of renal hereditary syphilis.

SANFORD, Chicago.

CERVICAL ADENITIS FOLLOWING VACCINATION WITH B C G. S. A. LOSTIĆ YOKSIĆ, Rev. franç. de pédiat. **7**:605, 1931.

The author reviews the literature, in which the first case was reported in 1928, and cites 7 cases from his own experience. In 5 of these cases it was proved that the cervical adenitis was initiated by the B C G vaccination. In the 2 cases last reported, suppuration occurred following vaccination with B C G, but other lesions were found. The vaccine was obtained from the Central Institute of Hygiene in Belgrade, and three doses of 400,000,000 organisms were given. These 7 cases were observed among 280 cases following vaccination. Yoksić does not believe that the occasional appearance of cervical adenitis should be a deterrent to the use of B C G, but rather that B C G vaccination should be reserved for infants likely to be exposed to tuberculosis.

SANFORD, Chicago.

SYPHILIS AS AN ETIOLOGIC AGENT IN BRONCHIAL DILATATION IN INFANTS. V. MIKULOWSKI, Rev. franç. de pédiat. **7**:651 (Oct.) 1931.

The author reports two cases of children with dilatation of the bronchi and positive Wassermann reactions. They both had varices, enlarged stomachs and other symptoms of hypophyseal derangement. While the dilated bronchi could have been caused by syphilitic action on the elastic tissue of the bronchi, the author presents the possibility of the effect of syphilis on the endocrine glands.

SANFORD, Chicago.

PRIMARY OSSEOUS ACTINOMYCOSIS. E. ALLENBACH, A. SARTORI and M. ZIMMER, Rev. d'orthop. **18**:572 (Sept.) 1931.

Actinomycosis enters the body either by way of the nose and mouth, producing a primary focus in the respiratory tract, or through a break in the skin. The entrance point through the skin is often so small that it passes unnoticed, and subsequent examination fails to discover the site of the primary focus. Spread of the disease beyond the primary focus can be either hematogenous or lymphogenous, and secondary nodules can locate either in the soft tissues or in bone, predominately in the long bones. Fifty per cent of the so-called primary bone foci occur in the lower limbs. In the authors' hands complete excision of the bone foci, followed by intense iodine treatment up to the limit of tolerance, has produced excellent results. Roentgen and radium treatment is of service in the more superficial lesions. Occasionally amputation or exarticulation will be necessary. In the diagnosis, differentiation must be made between tuberculosis and acute and chronic osteomyelitis.

RYAN, Vancouver, B. C.

ACUTE TUBERCULOUS PNEUMONIC INFILTRATIONS IN CHILDHOOD. THEOPHIL BAUMANN, Schweiz. med. Wchnschr. **45**:1076 (Nov. 7) 1931.

There is a form of pulmonary tuberculosis in childhood that is characterized by the abrupt onset of severe clinical symptoms and large pulmonary consolidations of the lobar type. Extreme dyspnea, a high fever, prostration, cyanosis and the classic physical and roentgen signs of lobar pneumonia are the striking

features. Within a week or two the dyspnea, prostration and, usually, the fever subside, but dulness and bronchial breathing persist and the child remains ill. Positive tuberculin skin reactions are consistently given. Tubercle bacilli are occasionally recovered from the sputum. It is a matter of many months, or years, before the consolidation clears. Either a large area of calcification or a cavity is left behind, usually with some evidence of tuberculosis in the opposite lung. The prognosis is poor, as the infection tends to become chronic. Sanatorium care, until the subsidence of physical signs, and pneumothorax are recommended.

This condition can be differentiated from lobar pneumonia by its protracted course, positive tuberculin reaction and history of previous tuberculosis, if obtainable. At the onset, the distinction may be impossible. "Epituberculosis" differs, in that it runs a more benign, shorter course, gives few signs and symptoms, in spite of a large roentgen shadow, and leaves no calcification or cavity after resolution. The author presents six illustrative cases. He explains their pathogenesis in terms of pulmonary invasion from a tuberculous focus during the "secondary stage" of childhood infection.

WOLMAN, Chicago.

CASE OF APOPLEXY FOLLOWING SUNSHINE TREATMENT IN A CHILD WITH CONGENITAL SYPHILIS. O. SAXL, Med. Klin. **27**:849 (June 5) 1931.

In a boy, 14 years of age, exposed to sunshine for five hours the picture of apoplexy developed. The process was possibly due to syphilitic damage of the arteries (endarteritis obliterans?). The symptoms were convulsions, glycosuria and hemiplegia. In a few days there was almost complete recovery.

ZENTAY, St. Louis.

ACETARSONE IN PREGNANCY AND IN NEWLY BORN BABIES. E. KLAFTEN, Med. Klin. **27**:1208 (Aug. 14) 1931.

Acetarsone is a valuable addition to the methods of treatment in syphilis. The author uses it particularly toward the end of pregnancy. By this method it is possible to introduce into the body large amounts of arsenic. It is also useful in pregnant women who have a temporary sensitivity to arsphenamine. In newly born infants it seems to give good results. It is particularly valuable in preventive treatment. The author states that in spite of the good results with acetarsone the older methods of treatment should not be entirely neglected.

ZENTAY, St. Louis.

THE COURSE AND PROGNOSIS OF NURSLING'S TUBERCULOSIS. E. ROMINGER and L. SZEGÖ, Monatschr. f. Kinderh. **51**:161 (Oct. 31) 1931.

The authors report cases of tuberculosis seen in their clinic from 1923 to 1931. No cases were observed in patients under 2 months of age; seventeen occurred in infants of from 3 to 6 months, thirty-one in infants of from 7 to 12 months and twenty-two in infants of from 13 to 18 months. The prognosis is strictly individual and depends on the massiveness of the first infection, virulence of the germ, age, constitution and environment. As several factors are involved in each case, it is difficult to determine the relative importance of the individual factors. The rôle of a second infection of tuberculosis implanted on the first is not clear. In general, the younger the child, the less favorable is the prognosis. The authors show x-ray pictures and give case reports to prove that the prognosis of tuberculosis in infancy is not necessarily hopeless. Many patients recover unless a meningitis or miliary tuberculosis develops. In fact, one might say that the prognosis depends on whether these complications develop.

GERSTLEY, Chicago.

THE IMMUNIZING EFFECT OF B C G. SLAVOJ VĚŠIN, Časop. lék. česk. **68:** 1683 (Dec. 6) 1929.

From work with guinea-pigs, the author concludes that B C G is not absolutely avirulent on the basis of specific tissue changes, which may include macroscopic caseation. These changes are found only in the first weeks following injection. No instance of death due to generalized infection was found. Doses of from 0.1 to 5 mg. did not produce changes much different from those in the controls, but minimal doses of 0.01 mg. produced a slower reaction with a greater tendency to heal. Complete immunity was not obtained with single phase doses of small caliber. The tuberculin reaction was inconstant. In the majority of animals doses of more than 1 mg. resulted in a positive reaction in ten days, but this was variable and might disappear in spite of other experimental evidence of a certain degree of immunity.

STULIK, Chicago.

ANTITUBERCULOUS VACCINATION OF THE NEW-BORN WITH B C G. VLADIMIR KRAL, Časop. lék. česk. **68:**1734 (Dec. 13) 1929.

The Calmette method of vaccination of the new-born was used in infants with tuberculous mothers, in infants with a history of tuberculosis in the family and in premature, congenitally weak and debilitated infants. A year after 160 infants were inoculated, a survey of 102 was made through the personal observation or written report of the local physician. Of 13 infants with tuberculous mothers none died, of 37 with tuberculosis in the family 5 died and of the 52 debilitated infants 8 died, a total death rate of 12.74 per cent. Of these, 6 or 5.88 per cent died of tuberculosis within six months, 6 or 5.88 per cent of other diseases within six months and one of rickets within a year. The death rate in France for tuberculosis in the new-born is from 23 to 26 per cent, but the general death rate in this district is 13.21 per cent, so that in comparison the death rate of the inoculated infants is a trifle lower. The conclusion is that B C G is not harmful for the new-born, is well tolerated and is of value in lowering the death rate.

STULIK, Chicago.

DEMONSTRATION OF TUBERCULIN IN THE CEREBROSPINAL FLUID. P. UJSAGHY, Orvosi hetil. **75:**939 (Sept.) 1931.

The best method for finding the acid-fast organism in the cerebrospinal fluid is centrifugating the fluid immediately after lumbar puncture. If web formation has already taken place, the only method left, which is not quite as reliable as the former one, is spreading the web on a slide. For staining of the slides, besides the Ziehl-Neelsen method, the method suggested by Spengler, Jotten and Haarmann can be used with good results.

ZENTAY, St. Louis.

Internal Diseases

FEMORAL ANEURYSM DURING SUBACUTE BACTERIAL ENDOCARDITIS IN CHILDHOOD. JOHN DORSEY CRAIG, J. A. M. A. **97:**245 (July 25) 1931.

In a boy, aged 10, suffering from subacute bacterial endocarditis a small tumor developed below the left Poupart ligament, which increased in size. A diagnosis of aneurysm of the femoral artery was made.

BONAR, Salt Lake City.

ACUTE LYMPHATIC LEUKEMIA IN CHILDHOOD: CASE REPORT WITH AUTOPSY. JAMES H. PARK, JR., South. M. J. **24:**670 (Aug.) 1931.

The author reports a case of lymphatic leukemia, occurring in a boy, with very unusual aspects. The case had a very sudden onset, was fulminating and showed an absence of generalized superficial adenopathy and complete lack of hemorrhagic manifestations.

SCHLUTZ, Chicago.

OBSERVATIONS ON THE CHLORIDE METABOLISM IN CONGENITAL PYLORIC STENOSIS. NOAH MORRIS and STANLEY GRAHAM, Arch. Dis. Childhood **6**:27 (Feb.) 1931.

In untreated pyloric stenosis there is a partial chlorine vacuum in the tissues. This can be corrected by the administration of saline, which, if continued, frequently leads to an excessive retention of chlorine and the production of edema, even when the chlorine content of the blood is normal. In such cases the chlorine content of the tissues is higher than normal. Restoration of the blood chlorine content to normal does not result in a correction of the alkalosis, as is evidenced by the persistence of the high total carbon dioxide content and the depressed breathing. A normal blood chlorine content may be accompanied by a fractional amount of chlorine in the urine. To permit of a satisfactory explanation of these findings, it appears necessary to postulate either (1) the inability of the kidney to excrete chlorine or (2) more probably, in view of the findings with urea and fixed base, the presence of chlorine in the tissues in a form other than BCl. Certain evidence is brought forward in support of the latter view.

KELLY, Milwaukee.

NUTRITIONAL ANEMIA IN INFANCY. HELEN M. MACKAY, Medical Research Council, Report no. 157, London, 1931.

The literature on the normal blood values of infants and their variations is reviewed. The review shows little recognition of the researches of American workers. The author's series on artificially fed infants numbered 174. They were fed a milk diet until 8 months of age, when they were given eggs, soup, gravy, vegetables, cereals and fruit. The daily dose of cod liver oil was three-fourths drachm. The iron given was iron and ammonium citrate with a trace of copper. This was incorporated in dried milk, and the daily quantity given was from 4½ to 9 grains (0.29 to 0.58 Gm.). In the infants treated with iron the hemoglobin content was raised after 3 months of age. It was found that by continuous medication the average hemoglobin content could be kept at a level of 77 per cent from 5 to 12 months of age. The infants given iron had a lower morbidity rate in both gastro-intestinal and respiratory infections. The gain in weight was also higher, averaging 1 pound (0.4 Kg.) more than the control group.

In 230 infants that were breast-fed until 7 months of age or over the average hemoglobin level every month was below that for infants given iron; the amount of hemoglobin was not different from that of untreated, artificially fed infants. Forty-four mothers were given antenatal treatment with iron. While the maternal hemoglobin was slightly increased, there was no effect on the infants' hemoglobin.

It was found that physical immaturity and anemia in the mothers predisposed to anemia in the child. In the infants it was found that prematurity, rapid gain and infections, as well as jaundice and edema at birth, decreased the hemoglobin. The author terms this anemia a nutritional anemia. The diagnosis is made by examination of the blood. She considers a drop below the normal value as an anemia. The normal is 100 per cent hemoglobin at birth, dropping to 70 per cent at 2 months and increasing to 80 per cent at 4 months. This figure is kept throughout the first year. These values are considerably above those given by most American investigators, and it should be understood that the author used Haldane's method of determination, 13.8 Gm. of hemoglobin per hundred cubic centimeters. American investigators have noted that the resulting percentage is 115 per cent, which is misleading. The author advises that all artificially fed infants and all breast-fed infants of a low birth weight should be treated prophylactically with iron for the first twelve months. This should be given by mouth as iron and ammonium citrate (1½ grains [0.09 Gm.] in 1 drachm of water or chloroform water, flavored with syrup). The beginning dosage should be a few drops a day increased to 1½ drachms or more three times a day. It was noted that liver therapy also causes a rapid rise in hemoglobin.

SANFORD, Chicago.

FAMILIAL ESSENTIAL THROMBOCYTOPENIA IN A BOY AGED SEVEN YEARS. L. J. WILTS and E. T. CONYBEARE, Proc. Roy. Soc. Med. **24**:709 (April) 1931.

A case of familial essential thrombocytopenia is reported in a boy of 7 years who had suffered from bleeding from the gums and excessive bruising since the age of 4. The blood count and family history are given.

WILLIAMSON, New Orleans.

TRANSMISSION OF INFANTILE LEISHMANIASIS. F. LO PRESTI-SEMINERIO, Arch. de méd. d. enf. **34**:386 (June) 1931.

Continuing a discussion of the etiologic factors in leishmaniasis of childhood, begun in a paper presented before the Sicilian section of the Italian Pediatric Society in November, 1930, Prof. F. Lo Presti-Seminerio amplifies his hypothesis regarding the rôle of insects in the transmission of the infective agent. Various ectoparasites, particularly the flea, the louse, the fly, the bed-bug and the mosquito, have been suspected of acting as an intermediate host for the Leishman-Donovan body. Zuccarelli and others believe in the canine origin of the disease and in the invasion of the intestinal tract of children; Beneveorte advocated the theory of a primary infection of the upper respiratory tract, from the almost constant bronchial irritation noted at the onset of this strange disorder.

In advancing the opinion that the common vector of kala-azar is the mosquito, the author answers the natural objection offered to this view, by assuming that although the various species of mosquito are numerous in Italy and malaria is extremely common, the parasite of leishmaniasis is so rarely seen in the peripheral blood, unlike the plasmodium, that few mosquitoes become infected and the danger of transmission is consequently greatly diminished.

AMESSE, Denver.

PULMONARY ABSCESS IN INFANCY: TREATMENT WITH EMETINE HYDROCHLORIDE. FERNANDO MARTILLOTTI, Pediatria **39**:707 (July 1) 1931.

The author reports a case of pulmonary abscess in a child of 4 years whom he successfully treated with hypodermic administrations of emetine hydrochloride. A review of the literature on the subject is carefully analyzed. His conclusions are summarized as follows: 1. Emetine hydrochloride in small doses is an excellent remedy for diseases of the respiratory tract and especially for pulmonary abscesses in children. 2. Urinalyses before and during the treatment and close observance of the patient's general condition are necessary points in the management of these cases. 3. It is an error to attempt to persist in the continuation of this treatment if no appreciable improvement follows the administration of the first series of six or seven daily doses. An exception to this rule applies to cases of amebic pulmonary abscess.

SIGNORELLI, New Orleans.

THERAPY IN ACUTE NEPHRITIS. HANS EPPINGER, Klin. Wchnschr. **9**:2043 (Nov. 1) 1930.

After a discussion of the physiology of the capillaries the author reports three cases in which diathermy was used. One was a case of mercuric chloride poisoning, and in the others nephritis followed angina. In the treatment, a lead electrode was used over the kidney and a large indifferent electrode on the abdomen, for from two to two and a half hours twice daily. The author believes that the good results were not a coincidence, and although there were many observations in which the results were not striking, he recommends that diathermy be tried in every acute case.

SILVERMAN, Syracuse, N. Y.

PATHOGENESIS OF ERYTHREMIA AND LEUKEMIA. F. PARKES WEBER and O. B. BODE, Klin. Wchnschr. **9**:2244 (Nov. 29) 1930.

Polycythemia that is secondary or due to a compensatory mechanism, such as lower oxygen pressure or congenital heart disease, may be designated as erythrocytosis, in analogy with leukocytosis. For conditions in which there is excessive hematopoietic, particularly erythroblastic, activity of the bone marrow the designation erythremia was chosen, in analogy with leukemia. The chief argument for the concept that in erythremia the main cause is the excessive erythroblastic activity of the bone marrow is the existence of a group of cases in which erythremia is combined with leukemia; that is, the blood picture shows an increase in white and red cells and histologically a combination of the characteristic changes in both diseases.

Erythroleukemia may be looked on as the early stage of a myelogenous leukemia before the exhaustion of the bone marrow leads to anemia. Cases of erythremia and leukemia may differ from one another, but all represent the links of a chain, at one end of which erythremia, and at the other end leukemia, represents excessive hematopoietic activity.

It presents the neoplastic theory as the most acceptable for the explanation of these conditions. The neoplastic process evinces itself as (1) erythremia when there is erythroblastic hyperfunction, (2) erythroleukemia when both erythroblastic and myeloblastic functions are involved, (3) erythremia followed by myelogenous leukemia when first the erythroblastic and then the myeloblastic activity is involved, (4) myelogenous leukemia followed by erythremia and (5) myelogenous leukemia when only myeloblastic hyperactivity is involved.

SILVERMAN, Syracuse, N. Y.

KURTEN'S TEST IN THE DIFFERENTIAL DIAGNOSIS OF ENDOCARDITIS LENTA. H. MAY, Med. Klin. **27**:16 (Jan. 2) 1931.

The differential diagnosis of endocarditis lenta is always difficult. Kurten's test seems to be a help in this problem. The method is as follows: 1 cc. of blood serum is mixed with 2 cc. of a 40 per cent solution of formaldehyde. The formaldehyde solution has to be neutralized for phenolphthalein by the addition of 20 per cent sodium carbonate. The mixture is left in a test tube at room temperature, and the coagulation is tested from time to time. The coagulation of the blood serum seems to be a reliable method in the differential diagnosis of endocarditis lenta and rheumatic endocarditis. Only in patients with a high temperature is it somewhat unreliable, as a negative result does not rule out the possibility of endocarditis lenta. Other conditions, such as syphilis and tuberculosis, cannot be ruled out by this method.

ZENTAY, St. Louis.

A NEW CONSIDERATION OF OSTEOGENESIS IMPERFECTA. ERNST JECKELN, Virchows Arch. f. path. Anat. **280**:351 (March) 1931.

The macroscopic and histologic observations in a typical case of osteogenesis imperfecta are described. The patient, who died shortly after birth, showed marked edema of the entire body. There were no changes in the ductless glands. The histologic picture of the bones and teeth as a most striking localization of the disease is discussed in detail. The author found remains of lamella of bone which can be present only if the osteoblasts are functioning normally. From this he concludes that in osteogenesis imperfecta there are periods of normal function of osteoblasts and odontoblasts alternating with periods in which a breakdown in the function of these cells occurs due to a primary inferiority of the mesenchyma.

SCHOENTHAL, New York.

LIPOID NEPHROSIS. A. R. KANTROWITZ and P. KLEMPERER, Virchows Arch. f. path. Anat. **280**:554 (March) 1931.

Using Mallory Heidenhain's azan-carmine stain in the histologic examination of the kidneys in four cases of lipoid nephrosis, Bell came to the conclusion that "lipoid nephrosis has to be considered as a form of glomerular nephritis in which the glomeruli are damaged, but their capillaries are only partially obstructed, so that they continue to function and tubular atrophy does not occur."

The authors examined the kidneys in two cases of lipoid nephrosis with the same technic. They were unable to detect any inflammatory changes in the glomeruli. The enlargement of the endothelial cells of the glomeruli which Bell considered as due to an inflammatory process they feel can be explained by the deposition of lipoid substance (lipemia) which is not specific for lipoid nephrosis and which was found in the kidneys of a patient who died of Niemann-Pick's disease. They therefore do not accept Bell's theory.

SCHOENTHAL, New York.

CLINICAL HEMATOLOGY IN CHILDREN. E. STRANSKY, Ztschr. f. Kinderh. **51**:111 (May) 1931.

An acute myeloid leukemia is described in a girl 6 years old, taken ill suddenly while in the best of health, and dead within five weeks. At first she showed the classic signs, hemorrhagic diathesis, stomatitis, fever and swelling of the glands and spleen, so that the diagnosis seemed easy. The leukocyte count, 55,000 at first, sank in a few days to 600. The constantly posterior oxydase reaction left no doubt but that morphologically the case was one of small cell myeloblastic leukemia. The differential count showed: eosinophils, 1.25 per cent; myeloblasts, 97 per cent (?); myelocytes, 0.25 per cent; young forms, 0.5 per cent; band forms, 1 per cent; segmented cells, 0.5 per cent, and lymphocytes (?). The case was peculiar in its rapid course, and in the sudden sinking of the number of leukocytes from an unknown cause.

A case of lymphogranulomatosis in a boy, observed for one and a half years (between the ages of 8¼ and 9¾ years), was distinguished by an erythroblastosis, anemia and swelling of the glands and spleen. The blood cleared up, the swelling went away under roentgen treatment and the boy remained well for about one year. He became sick again, but this time received no benefit from x-rays. This was an anemia of the aplastic type. Examination of the blood showed: red cells, 2,314,000; hemoglobin, 32 per cent; white cells, 4,500; basophils, 0.5 per cent; eosinophils, 3 per cent; myelocytes, 0.5 per cent; young forms, 1.5 per cent band forms, 25 per cent; segmented cells, 42 per cent; lymphocytes, 24.5 per cent, and monocytes, 3 per cent. Erythroblasts numbered 8 per hundred cells. A transfusion of blood resulted in a transient erythroblastosis. Up to the present, improvement in the blood and the general condition has been lasting.

EMERSON, Boston.

TROPHONEUROTIC HYPERTROPHY OF ONE EXTREMITY CAUSED BY A CALCIFIED DESCENDING ABSCESS. M. MARCUS and H. VOLLMER, Ztschr. f. Kinderh. **51**:127 (May) 1931.

A case of tuberculosis of the lumbar vertebrae is reported in a boy 8 years old, who had a calcified abscess which extended down and under Poupart's ligament. On the diseased side, the leg was greatly hypertrophied, a condition that is assumed to be trophoneurotic, caused by the pressure of a calcified mass for years on the lumbosacralis plexus, in a period of active growth of the body.

EMERSON, Boston.

GOITER AMONG SCHOOL CHILDREN IN THE FOURTH ADMINISTRATION DISTRICT OF BERLIN. F. HEIMANN, E. ISRAELSKI and J. SIMSON, Ztschr. f. Kinderh. **51**:195 (June) 1931.

The study of 15,351 children in the fourth administration district of Berlin as to the extent of goiter gave a frequency of 3.2 per cent among boys (total number, 7,189) and of 4.8 per cent among girls (total, 8,162). A mild swelling of the thyroid was noted in 15.3 per cent of the boys and in 17.1 per cent of the girls. Universal iodine prophylaxis is therefore superfluous.

EMERSON, Boston.

THE CLINICAL DIAGNOSIS OF CONGENITAL HEART DISEASE. G. VONBERG, Ztschr. f. Kinderh. **51**:221, 1931.

Vonberg reports one case of Roger's disease and one of open ductus arteriosus, the discussion of which is very helpful but is not easily abstracted. The original may be read with profit by those who are interested in the diagnosis of congenital heart disease.

EMERSON, Boston.

ESOPHAGOSPASM IN CHILDREN. H. BRÜHL, Ztschr. f. Laryng., Rhin. (Teil 1: Folia oto-laryng.) **21**:1 (June) 1931.

Brühl first gives several case histories of children with esophagospasm. That the disturbance was really localized in the esophagus is proved by the typical sign, namely, that the food is regurgitated without nausea, immediately after swallowing. The process is more of an outflowing than an actual gastric vomiting. It is usually combined with irritative coughing and a feeling of oppression. The vomitus does not yet show the influence of the gastric hydrochloric acid. In the cases under the author's observation the roentgen examination always corroborated the clinical diagnosis, and the location of the esophageal obstruction could be exactly localized. The onset of the disturbance disproves the congenital character; esophageal neoplasms are almost unknown during childhood, and the obstruction of the esophagus by mediastinal processes can be excluded on the basis of the anamnesis, the clinical behavior and the roentgen picture. More difficult is the differentiation between organic stenosis and spasm. In the two last cases described by the author the mode of onset, the sudden changes in the clinical behavior, and the effectiveness of pedagogic measures indicated a functional disturbance. In the first case reported, in which the esophagospasm developed after the drinking of a corrosive fluid, there was a slight cicatricial stenosis, for in contradistinction to the two first cases the introduced sound encountered a certain surmountable obstacle. The further course was similar to that in the other two cases. Before discussing the pathogenetic mechanism of spastic esophageal stenosis the author reviews the anatomic structure of the esophagus, its innervation, its peristalsis and the complicated reflex process of swallowing, and he points out that the normal esophageal action consists of a complicated bulbar reflex, which is similar to the simple spinal reflex arcs. Changes in the peripheral organ, as, for instance, corrosion of the esophagus, may cause a reflex increase. The author further discusses the esophagospasm that develops as the result of an irritation of the peripheral neuromuscular synapses, as in cases of tetany, following attacks of pertussis and in chorea. All these cases of esophagospasm are similar in pathogenesis and are of the sensomotor type. In another form of esophagospasm psychic factors are involved. Because of the connection of the peripheral reflex disturbance with central psychical processes this group is designated as correlative esophagospasm, and has the aspects of a traumatic neurosis. In the third, purely psychogenic form, the hypobulic mechanism is involved. In discussing the therapy of esophagospasm the author emphasizes the significance of psychotherapy, especially for the neurotic and psychogenic forms. The main object should be to treat the

child and not the esophagus. It is usually of great help to bring the child into different surroundings and to employ "physiologic bougienage," the food itself serving as bougie. The esophagus is trained by gradually increasing the amounts and the variety of foods. In some cases, of course, this method fails, and surgical treatment becomes necessary.

EDITOR'S ABSTRACT [ARCH. OTOLARYNG.].

FRAGILITY OF THE BONES, BLUE SCLERAE AND AURICULAR DISTURBANCES. V. TANTURRI, Ztschr. f. Laryng., Rhin. (Teil 1: Folia oto-laryng.) **21**:115 (June) 1931.

Tanturri directs attention to a familial syndrome in which fragility of the bones, blue sclerae and auricular disturbances concur. Studies on the members of a family in which this syndrome was hereditary convinced him that the disturbances of the middle and internal ear are probably caused by otosclerotic foci. The disorders of the ear were, in most cases, accompanied by endocrine disturbances, such as amenorrhea, dysmenorrhea and hyperthyroidism. On the basis of his observations the author reaches the following conclusions: 1. In every case of osteopsathyrosis a careful examination of the ear should be made, for usually there are latent disturbances of the cochlear and especially of the vestibular apparatus. 2. The disorders in the region of the internal ear (ampullar unresponsiveness), which may be considered as neurosensorial, are most likely caused by otosclerotic foci of atypical location, for in the same family there are persons with symptoms of the internal ear and persons with typical otosclerosis. 3. It appears that the position reflexes (nystagmus without vertigo) do not depend on the peripheral disturbances of the otolith apparatus, but seem to belong to a category of reflexes of nervous origin, probably entirely independent of the otolithic system, and connected with conditions of the nervous, cerebrospinal and sympathetic systems. 4. The endocrine disturbances that were observed in the patients justify the hypothesis that correlations exist between the disturbances of the bones, of the ears and of the endocrine glands, so that osteopsathyrosis, otosclerosis and other diseases of the bones may be classified as dystrophic diseases caused by biochemical disturbances.

EDITOR'S ABSTRACT [ARCH. OTOLARYNG.].

AGE VARIATIONS IN THE EFFECT OF ORALLY ADMINISTERED INSULIN. M. HASEGAWA, J. Pediat. (Tokyo), July 20, 1931, no. 374, p. 1016.

The author administered insulin (Lilly) by mouth to rabbits of various ages in conjunction with physiologic solution of sodium chloride. He found that by so administering insulin, the effect of lowering the blood sugar value is definite, and that the younger the animal, the more rapid are the fall and the restoration to the normal. Insulin, however, given in this way is not as effective as that given by subcutaneous injection.

KATO, Chicago.

OPISTHOTONOS IN EMPYEMA, A SIGN NOT DESCRIBED BEFORE. Y. NAGAO, J. Pediat (Tokyo), July 20, 1931, no. 374, p. 1067.

Nagao describes several cases of empyema in which opisthotonos, or a bowing of the head and trunk backward, as if the patient were suffering from some variety of meningitis, were observed. The Brudzinski and Kernig signs are usually negative in these cases. The author thinks that this phenomenon appears whenever the patient has a rather large amount of purulent material in the chest, so that the shadow or dulness extends up to the upper part of the thorax, either unilaterally or bilaterally. The symptom disappears when the pus is drained adequately.

KATO, Chicago.

INTESTINAL WORMS ON TERSCHELLING. J. H. SCHUURMANS STEKHOVEN, JR., Nederl. tijdschr. v. geneesk. **75**:859 (Feb. 21) 1931.

The author studied the intensity of infection with Ascaris and Trichocephalus trichiura at Midsland on the island of Terschelling (Holland). Ascaris infection was found in 36.7 per cent of the persons examined, and Trichocephalus trichiura in 53.1 per cent. On other parts of the island the infection was much more frequent. After the fifteenth year of life the intensity of the infection generally decreased.

VAN CREVELD, Amsterdam, Holland.

A PECULIAR FORM OF ASCARIASIS. S. VAN CREVELD, Nederl. tijdschr. v. geneesk. **75**:890 (Feb. 21) 1931.

A form of ascariasis is described, characterized by a combination of the following symptoms: 1. Eggs are absent from the stools, or only a few degenerated ones are present. 2. Eosinophilia is absent. 3. The Ascaris, which was finally expelled with the stool, resisted a great many different forms of treatment for worms. 4. The presence of Ascaris in the intestines gave rise to severe hemorrhages and probably also to one attack of ileus. 5. A severe anemia developed. 6. Several general symptoms of intoxication were found (clubbed fingers and toes, especially), which slowly disappeared after the excretion of the Ascaris, as did the anemia. 7. This Ascaris had poorly developed sexual organs, containing only a few degenerated eggs; in the intestine of the worm, destruction products of the blood could be demonstrated.

VAN CREVELD, Amsterdam, Holland.

DIABETES MELLITUS. E. GORTER, Nederl. tijdschr. v. geneesk. **75**:1076 (Feb. 28) 1931.

The author gives his experience in the treatment of children for diabetes mellitus. The blood sugar is determined a few times during the day while the patient is receiving his usual diet and insulin. A simple diet regulation is recommended. The influence of an infection on the general condition of the diabetic patient is once more stressed. Hypoglycemia cannot always be prevented, and may easily occur. Often suprarenal preparations are given which have an antagonistic influence on the blood sugar. In judging abnormalities in the blood sugar curve, one must pay attention to the different activity of the insulin preparations. Experience has shown that as the diabetic child gets older he nearly always needs more insulin. An important factor in the development of coma is the failure to give more insulin during an infection. Finally, three cases of familial renal glycosuria in children are discussed.

VAN CREVELD, Amsterdam, Holland.

GAUCHER'S DISEASE. C. DE LANGE, Nederl. tijdschr. v. geneesk. **75**:2037 (April 18) 1931.

In this article the author gives the history of two cases of Gaucher's disease in sisters. Both showed signs of hemorrhagic diathesis. Splenectomy was done in one of the children, and a detailed description of the histologic investigation of this spleen is given. De Lange's conclusion, in accordance with that of de Josselin de Jong, Pick and others, is that the sinus endothelium has no significance in the building of the large Gaucher cells. The literature on the histology of the disease is discussed in detail, and the author also gives the clinical and chemical facts obtained in recent years in investigations of Gaucher's and related diseases (Niemann-Pick's disease, lipoidosis of Schüller-Christian). The relation to the amaurotic family idiocy of Tay-Sachs is also discussed. The author believes that a differentiation between Niemann-Pick's disease and a form of Gaucher's disease occurring only in babies is justified, and she gives the clinical and histologic differential diagnosis. Some suggestions for further pathologic examination of Gaucher's and related diseases are given.

VAN CREVELD, Amsterdam, Holland.

Nervous Diseases

AMYOTONIA CONGENITA: REPORT OF TWO CASES IN THE SAME FAMILY. EDWARD L. BENJAMIN, Arch. Pediat. **48**:734 (Nov.) 1931.

The author's summary is as follows: "1. Two cases of myotonia in the same family are presented because of the striking features in both and the familial tendency. 2. In both instances, the children were unable to stand or walk before the second year. 3. Both showed the characteristic hypotonicity of the muscles of the lower limbs and also a disproportion between hips and torso, which may be only a coincidence or a familial physical trait, but may also have some significance in relation to the development of the lower limbs. 4. Like many families, this particular one showed a familial retardation which was characteristic on both the maternal and the paternal sides. 5. Both cases improved rapidly under general tonic treatment as do most of those of the benign type."

WADDELL, University, Va.

HEREDITY AND MENTAL DEFICIENCY. PAUL POPENOE, Ment. Hyg. **15**:570 (July) 1931.

The reversion of several geneticists to the old idea that feeblemindedness is a unit characteristic is lamented by Popenoe. The author acknowledges that in the lower levels of the intelligence scale there is a qualitative rather than a quantitative difference, and that an idiot differs in kind rather than in degree from a well rounded genius. But the bulk of scientific evidence points away from the unit character theory. Feeblemindedness itself is a largely undefinable concept, concerned as it is with social adjustment rather than biologic characteristics. Goddard's pioneer work, such as his study of the pedigree of the Kallikak family, is based on the uncertain foundation of subjective estimates by friends, workers and neighbors. Since to begin with there is no clearcut concept of feeblemindedness, all studies that divide rigidly the normal from the mentally defective are necessarily inaccurate. Popenoe hastens to remark that he does not doubt that feeblemindedness is inherited; what he questions is the way in which this transmission occurs. He concludes with an expression of approval of the program of the eugenists to limit the offspring of the mentally defective and encourage the breeding of the superior.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.].

THE MOTOR AND NEUROLOGIC DEVELOPMENT OF THE INFANT. E. PICHON, Paris méd. **1**:38 (Jan. 9) 1932.

A résumé of the usually accepted theories on development is presented.

SANFORD, Chicago.

CLINICAL OBSERVATIONS ON EPIDEMIC CEREBROSPINAL MENINGITIS, WITH SPECIAL REGARD TO RESULTS OF TREATMENT. B. VASILE, Pediatria **39**:793 (Aug.1) 1931.

During the past two years there has been a wide prevalence of cerebrospinal meningitis in and about Palermo. The mortality in thirty-three cases under discussion was unduly high (70 per cent). This high mortality is attributed to inefficient response of the disease to serotherapy, unless serum prepared from the particular strain of the micro-organism responsible for the disease is used, when the results are more satisfactory. The author recommends the use of serum developed from the strain of the micro-organism producing the disease.

SIGNORELLI, New Orleans.

MODIFICATIONS OF THE CEREBROSPINAL FLUID IN CHILDREN TREATED WITH ULTRAVIOLET RAYS. G. A. PIANA, Riv. di clin. pediat. **29**:553, 1931.

Eleven healthy children between 4 months and 8 years of age were used in this study. The spinal fluid was withdrawn before and after a course of irradiation totalling from six to eight hours' exposure over a period of from fifteen to twenty days. Essentially no change was noticed in the appearance, pressure, p_H or cell count. The albumin, sugar, calcium and inorganic phosphorus were constantly higher in the fluid obtained following irradiation; the chloride was lower. The author points out that changes in the spinal fluid parallel similar changes in the blood.

HIGGINS, Boston.

THE DEXTROSE, LACTIC ACID AND PHOSPHORUS OF THE CEREBROSPINAL FLUID. G. DE TONI, Scritti med. dedicati a Carlo Comba, ediz., Riv. di clin. pediat., 1929, p. 578.

In fourteen normal infants the spinal fluid contained an average of 0.068 per cent dextrose (maximum, 0.083 per cent; minimum, 0.056 per cent), 0.017 per cent lactic acid (maximum, 0.021 per cent; minimum, 0.012 per cent) and 0.0013 per cent phosphorus (maximum, 0.0016 per cent; minimum, 0.0008 per cent).

In children with congested meninges (meningismus), as in tumor of the brain, pneumonia and spasmophilia, the sugar in the spinal fluid was usually a little increased (from 0.080 to 0.117 per cent), while the lactic acid and phosphorus were normal.

In children with tuberculous or purulent meningitis, the sugar in the spinal fluid was markedly diminished (frequently absent in the purulent type), while the lactic acid was considerably increased (0.063 per cent) and the phosphorus (0.0024 per cent) was also increased.

In children with active rickets, the sugar in the spinal fluid was normal, but the lactic acid (0.015 per cent) and phosphorus (0.0010 per cent) tended to be low.

The phosphorus of the spinal fluid is wholly inorganic. The lactic acid of the spinal fluid comes from two sources: (1) diffusion from the blood and (2) breaking down of the sugar of the spinal fluid.

HIGGINS, Boston.

ACUTE ENCEPHALITIS IN CHILDHOOD. A. GAREISO, Arch. argent. de pediat. **2**:31 (Jan.) 1931.

The author presents a discussion of the various forms of acute encephalitis in childhood: their etiology, symptomatology, pathology and complications. He brings out the fact that all toxic and infectious conditions, specific or nonspecific, localized or generalized, may produce an encephalitis. Reference is also made to the encephalitic lesions produced by the cerebral form of Heine-Medin disease. The author also emphasizes the complexity and polymorphism of postencephalitic symptoms, the close relationship of certain forms of epilepsy and Sydenham's chorea to encephalitis, and finally the importance of a detailed history, which may frequently explain a great number of vague nervous conditions.

SCHLUTZ, Chicago.

THE TECHNIC OF CISTERNAL PUNCTURE. O. GAUSS, Deutsche med. Wchnschr. **58**:14 (Jan. 1) 1932.

Gauss believes that cisternal puncture should not be done by general practitioners. However, if performed by an expert in a hospital, this is the simplest and, from the point of view of the patient, the most agreeable method of collecting cerebrospinal fluid. The author describes a sign for the determination of the depths of the inserted needle. If the needle has passed the resistance of the ligamentum nuchae, but has not as yet passed the membrana atlanto-occipitalis and dura mater, the needle has play and can be pushed in and out a little bit with

ease. The skin forms a cone around the movable needle, which forms the apex of the cone. However, if the resistance of the membrana atlanto-occipitalis and the dura is passed, the needle no longer has any play but is well anchored in two places. Occasionally one experiences another resistance before reaching the cisterna; this is the resistance of the epidural venous plexus. On withdrawing the needle, one notices again the play of the needle and the cone formation of the skin; as soon as the needle is outside the membrana atlanto-occipitalis and the dura it is anchored by only the ligamentum nuchae.

KERESZTURI, New York.

EXSICCOSIS IN ACUTE CEREBRAL DISEASES OF THE INFANT. E. SCHIFF, Jahrb. f. Kinderh. **132**:129 (July) 1931.

Whenever an infant, apparently in good health or in the late stage of convalescence, who has received adequate diet suddenly develops vomiting, diarrhea, fever and dehydration that resist treatment, and when the history and examination reveal no cause for the symptoms, Schiff considers the possibility of acute cerebral disease, even if the cerebrospinal fluid and eyegrounds are normal. He presents a case of circumscribed meningitis, one of encephalitis, one of thrombosis of all the cerebral veins and one of metastatic meningitis — each without symptoms or signs of nervous disease. He believes that the localization of these infections is of no importance; but that the symptoms are caused by injury to the capillaries.

CLAUSEN, Rochester, N. Y.

THE CONGENITAL "CEREBRAL" FORM OF DYSTROPHIA ADIPOSOGENITALIS (LAURENCE-BIEDL SYNDROME). H. WILLI, Jahrb. f. Kinderh. **133**:12 (Sept.) 1931.

Two children of related parents presented this syndrome: dystrophia adiposogenitalis, visual disturbance and syndactylism. Both showed myopia, astigmatism, defects of the macula and lessened discrimination of color; one had typical retinitis pigmentosa, and the other, marked congenital coxa vara. In a third case, described by Denzler ten years previously, normal primary and secondary sex characters had developed. In all cases the sella turcica was enlarged, and all the patients were below average intelligence. The basal metabolic rate and specific dynamic response to protein were low. It seems likely that the hereditary factors are linked or carried by a single chromosome.

CLAUSEN, Rochester, N. Y.

THE RUDIMENTARY NEUROPSYCHIC FUNCTIONS OF THE INFANT. J. S. GALANT, Jahrb. f. Kinderh. **133**:75 (Sept.) 1931.

The Babinski reflex is considered as a rudiment of the grasping reflex useful to the ape. Other rudimentary reactions of the infant include the "storm of activity," occasioned by bodily discomfort, and destructive play. All these rudiments are lost in normal development, but may reappear in hysteria, dementia praecox, dementia paralytica, etc., as pathologic "degenerate" reflexes.

CLAUSEN, Rochester, N. Y.

DIAGNOSTIC AND PROGNOSTIC SIGNIFICANCE OF SUGAR IN THE CEREBROSPINAL FLUID IN CHILDREN DURING AN INFLAMMATORY PROCESS OF THE MENINGES. T. MAGILNICKI, Pediat. polska **14**:153 (May-June) 1931.

The author states that normally one finds about 50 mg. of sugar per hundred cubic centimeters of cerebrospinal fluid; yet in the course of disease of the meninges the sugar content may be decreased or increased, depending on the type of disease. For example, sugar runs high in Heine-Medin disease, fevers associated with chills, tumor or hemorrhage of the brain, psychic diseases and in the agony of

death. A study was made of 217 children and 516 tests were performed by the same technician. He found that in tuberculous meningitis particularly the sugar content was low, fluctuating between 10 and 35 mg. per hundred cubic centimeters. The sugar content always diminishes when the condition becomes worse and before death. In the irritative type of meningitis the sugar content was found to be either normal or increased. This point is of great diagnostic importance as to whether an inflammatory process or just an irritative type of meningeal disease is present.

KRUPINSKI, Chicago.

THE ANATOMIC BASIS OF SLEEP. V. E. MICHEEV, J. nevropat. i psikhiat. **1**:75, 1931.

Five cases of tumor of the brain were reported in which sleepiness was the most prominent feature. In all the cases at autopsy there were tumors in the vicinity of the fourth ventricle. Of course, tumors frequently cause somnambulance in patients as a result of the increase in intracranial pressure, but even a slight involvement in the region of the fourth ventricle causes disturbances in sleep. The author believes that sleep is regulated by a rather large area extending from the fourth ventricle to the optic thalamus. He discusses the various theories of sleep, especially those advanced by Pavlov and his school. He cites an extremely interesting experiment of Krilov, who was able to induce deep sleep in a dog by the administration of chloral hydrate through a rectal tube. After the dog had been accustomed to the experiment the mere preparation for the procedure induced sleep. Injections of warm water also produced sleep. The author believes that sleep is a function of the organism as a whole, with the midbrain acting as a regulator of sleep and of wakefulness.

KASANIN, Howard, R. I. [ARCH. NEUROL. &. PSYCHIAT.].

BIRTH TRAUMA AND EPILEPSY. E. RYDBERG, Acta psychiat. et neurol. **6**:213, 1931.

The author has studied the lives of forty-nine children who showed definite evidence of intracranial trauma at birth and who are now at least more than 2 years of age. He reports in detail two cases in which there later developed convulsive seizures. He classifies the forty-nine patients as follows: (1) idiots and imbeciles (including twelve epileptic patients), twenty; (2) epileptic persons without defective intelligence, six (five?); (3) patients with spastic paralysis without defective intelligence or epilepsy, two; (4) infants with disturbances affecting the neuromuscular apparatus of the eyes, but without other defects, seven; (5) infants who died so early that nothing was known of the extent of the injury, two; (6) infants who died at a very early age, but in whom epileptic attacks had already occurred, two, and (7) healthy infants, ten.

It will be noticed that twenty infants had epileptic attacks. These attacks are often of the jacksonian type, or are characterized by the fact that the cramps are localized. Cases occur in which the convulsions are general, as well as those accompanied by fits of unconsciousness without convulsions. Aura and petit mal have been mentioned in one or two cases. This form of epilepsy has the general characteristics of what is known as secondary epilepsy. However, although local signs of cranial injury may not be pronounced, the author believes that even in cases in which the convulsion is general there are features that distinguish this form of disease from "genuine epilepsy." A characteristic feature of the latter disease is a brief period of convulsions followed by deep coma. Traumatic epilepsy, and even that produced by a birth trauma, is characterized by the fact that the attacks are frequently of much longer duration; in some of these cases, for instance, they have lasted for hours. Even during severe attacks the patient may retain consciousness and afterward remember the attack. If it is added that most patients with epilepsy due to a birth injury show other defects that can be traced back

to a very early age, it is obvious that in its essential features and in the great majority of cases this form of disease differs from primary epilepsy. Of the twenty cases in which epileptic fits occurred, there is not one that has presented such symptoms as would lead a physician to diagnose it as a case of genuine epilepsy, even if he were not aware of the existence of a birth injury.

PEARSON, Philadelphia [ARCH. NEUROL. & PSYCHIAT.].

CELL COUNT AND PROTEIN CONTENT OF THE SPINAL FLUID IN EPILEPSY. AXEL V. NEEL, Acta psychiat. et neurol. **6**:221, 1931.

The author attempted to correlate the spinal fluid findings in 381 cases of epileptiform convulsions, with the aim of elucidating to what extent one may ascertain the cause of the epilepsy in any particular case by an examination of the spinal fluid. He divided the cases into two main groups: I, in which examination did not reveal any definite cause for the convulsions, and II, in which the symptoms were suggestive of such a cause. In group I the total protein content falls very evenly around the dilution value 6, whereas in group II a very large number of cases show an increase in the total protein content. As a rule, there is no marked increase in globulin in either group. The cell count is higher in group II than in group I. The main result of this study showed that the spinal fluid is normal in the forms of epilepsy in which there is no demonstrable external cause, normal even to the strictest requirements. Quite the opposite applies to group II. If the cases of group I are tabulated according to the number of years the disease has lasted, the moderate pathologic changes are somewhat more frequent in old cases, with a duration of illness of thirty years or more, than in cases of from ten to fifteen years' standing. On the other hand, in old cases with pronounced psychic changes, the spinal fluid is often perfectly normal. Cases of recent origin, with a duration of the illness for six months or less, show relatively slight changes. He concludes that one is justified in claiming that by examination of the cell count and the protein content of the spinal fluid one may obtain some important data for the estimation of a case of epilepsy. If one finds the spinal fluid perfectly normal, this will suggest strongly that there is no organic brain lesion. When, on the other hand, a change is demonstrated, it would be a sure indication of the presence of an organic brain lesion, so that such a case of epilepsy, as a rule, would have to be considered symptomatic.

PEARSON, Philadelphia [ARCH. NEUROL. & PSYCHIAT.].

THE SUGAR CURVE IN THE CEREBROSPINAL FLUID AFTER THE ORAL ADMINISTRATION OF DEXTROSE. AUDUN SCHJÖTT, Acta psychiat. et neurol. **6**:247, 1931.

The author studied 117 cases. Of these, 16 were cases of cryptogenic epilepsy. In all except the epileptic cases the increase of sugar in the spinal fluid began from one and one-half to two hours after the oral administration of dextrose; the increase continued and reached its maximum from two and one-half to three hours after the administration, whereupon there followed a slow decrease to the original amount. In 13 of the 16 cases of cryptogenic epilepsy, there was an increase in the sugar of the spinal fluid, which greatly exceeded the increase found in all the other conditions, and which also began considerably earlier.

PEARSON, Philadelphia [ARCH. NEUROL. & PSYCHIAT.].

Miscellaneous

THE DANGERS AND ADVANTAGES OF SEX INSTRUCTION FOR CHILDREN. KARL DE SCHWEINITZ, Ment. Hyg. **15**:561 (July) 1931.

Facts represent no prophylactic against sexual misbehavior, and merely telling the child the details of sexual function is no assurance that he will have no mal-

adjustments in this field. De Schweinitz pleads for a less somber, less pedantic, less serious approach to the problem. There is, he insists, no need of holding an interview when the "facts of life" are told to an embarrased child by a still more embarrassed parent. Rather, let the child's questions be answered naturally and casually when they arise. He expresses the formula for happy child guidance as being an instruction to parents to "love them, set them a good example, and leave them alone."

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.].

PROBLEMS IN CHILD GUIDANCE. E. K. CLARKE, New York State J. Med. **30**: 1271 (Nov. 1) 1930.

The child guidance clinics that have developed under the mental hygiene movement are making rapid strides in research and preventive work. They are much in need of the cooperation of the pediatrician. He can assist by making thorough physical examinations, and the clinic can, in turn, assist him by taking over time-consuming psychiatric problems. In each case a complete physical examination and a psychologic and psychiatric study are made, and a social history obtained.

Two school classes have recently been established, one for preschool children presenting behavior problems and the other for children between 8 and 12 years of age. The latter are the children who disrupt the ordinary classroom. Good results have been obtained in both classes.

AIKMAN, Rochester, N. Y.

BRAZIL SOCIETY OF PEDIATRICS. Arch. de pediat., Rio de Janeiro, **27**:74 (Dec.) 1930.

Dr. Octavio de Veiga reported an increase in the number of cases of farinaceous dystrophy due to the substitution of farinaceous for lacteal alimentation. Dr. Edgar Filgueiras observed that in the Vital Institute of Brazil, Ramon's antitoxin did not always confer immunity after three doses; some patients still gave a positive Schick reaction after forty-five days. Dr. Martinho da Rocha commented that pemphigus of the new-born is met principally among children of syphilitic, alcoholic or otherwise debilitated parents.

OLIVER, Columbus, O.

THE SEROLOGIC DIAGNOSIS OF PATERNITY OF ZANGEMEISTER. ERNST GROS, Ztschr. f. Geburtsh. u. Gynäk. **99**:387, 1931.

The author tested the serologic diagnosis of the paternity of Zangemeister. He could not find a similar reaction in all investigations of the mixed serum of mother and child by the "Stufenphotometer," as claimed by Zangemeister. However, he observed the same results as Zangemeister when he tested the diminution of transparency in the investigations with mixed serum of father and child and of mother and father. Therefore some of his findings were incompatible with those of Zangemeister, while others were confirmatory.

ADAIR, Chicago.

CHILD'S PLAY AS AN ELEMENT OF SANITARY BREEDING. B. M. POLINSKY, Omat det i ozdop **3-4**:80, 1930.

Play has an important part in bringing up children. In itself, play is harmless and helps the child to acquire certain sanitary habits. Indoor amusement places must be established, and the children must be watched during play. Most young children playing with toys have a habit of putting them in their mouths. The toy that is painted with a harmful paint or is soiled does the child much harm. Play must be organized for the older child too. It should have a tendency to stimulate intelligence.

KRUPINSKI, Chicago.

Society Transactions

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

Nov. 14 and 15, 1930

W. D. Lyon, M.D., Presiding

Abdominal Pain.

Drs. Thomas D. Gordon, W. D. Lyon, Campbell Harvey, George Irving, J. P. Parsons and D. M. Cowie discussed the subject of abdominal pain in infancy and childhood. The importance of differentiation was stressed. It was pointed out that functional disturbances are responsible for a large percentage of the cases. Appendicitis, intestinal obstruction of various degrees, abdominal migraine, enterospasm and allergy were discussed.

Nutritional Anemia (Preliminary Report). Dr. A. Luvern Hays.

Thirteen cases of nutritional anemia were studied. The ages of the patients varied from 12 to 21 months. There were three twins and two premature infants. Three patients were exclusively breast fed for eleven, eight and eight months, respectively. The majority had received no vegetables in their feeding; a few had taken them in minimal amounts. None had received egg; only one had received meat. Vitamins were received irregularly.

These patients were susceptible to infections of the upper respiratory tract. In two pyelitis developed. None had syphilis or tuberculosis. Physical examination showed mainly pallor and malnutrition. The liver was just palpable; the spleen was not. Dentition was delayed in every patient except one. Edema was present in one patient.

The anemia was of the secondary type, the color index being below one. Hemoglobin ranged from 13 to 55 per cent. The red counts ranged from 2,150,000 to 4,600,000. The red cells showed achromia. In seven patients there was leukocytosis. A lymphocytosis as high as 70 per cent was found in some patients. The platelets were increased.

These patients were treated by (1) a high caloric, high vitamin, baby soft diet and ultraviolet rays, (2) transfusion, (3) iron and transfusion and (4) iron. Conclusions made after treatment were: Response can be obtained to diet alone, but it is slow. Response is most rapid to transfusion followed by iron. Massive doses of iron give almost as quick a response. Soluble or insoluble forms of iron can be used. Response to iron is obtained in two weeks. Transfusion causes immediate response.

DISCUSSION

Dr. Raphael Isaacs: When we talk about nutritional anemia, we must remember that the anemia is but one symptom of a process that is affecting every cell in the body. All the cells in the body contain iron, and if there is an iron deficiency, every cell in the body must be abnormal. At birth the organs contain a supply of iron sufficient to supply the needs of the developing body for from six to nine months. When the baby lives on milk for a long period, there may be certain changes in the blood—too few red cells or too little hemoglobin. When the diet is defective, the bone marrow tries to make up for the deficiency by the production of more blood cells than normal; later there is not enough actual substance to produce red cells, and immature and abnormal forms are noted.

When iron is fed as iron and ammonium citrate, U. S. P. (50 per cent solution), 4 cc. twice daily, or 4 Gm. of reduced iron daily, no effect is noted for

two weeks or longer. The iron, when absorbed, has no effect on the cells already in the blood stream, but affects those which are being made, the nucleated red cells.

When a blood transfusion is given, the bone marrow does not have to work so rapidly, and the cells can remain in it until they get a little riper. When the effect of the transfusion wears off, the bone marrow delivers the cells into the blood stream.

DR. HENRY PONCHER: I have found that the biggest drop in the hemoglobin occurs around the third or fourth month of life. Another decided drop may occur around the sixth or seventh month. Very few of our children with advanced rickets showed anemia. Premature infants do not recover like normal children after the drop in hemoglobin occurs. The supply of iron in the liver is small; evidently the premature patients are not capable of recovery. I have not found that any specific form of iron is better than another.

FAT TOLERANCE AS A FACTOR IN MALNUTRITION. DR. WILLIAM D. LYON.

The author discussed fat intolerance as it occurs in older children. Inability to digest and assimilate fats may arise through overfeeding in the first two years of life or, more often, may be secondary to various infections. Children so affected are malnourished and pale. A diet low in fats with gradual return to normal proved a satisfactory form of treatment.

THE RÔLE OF PROTEIN IN DIARRHEAL DISEASES. DR. PAUL B. KREITZ.

The author discussed the treatment of diarrhea and reviewed the various chemical changes and changes in body fluid occurring in the diarrheas of infancy.

CONGENITAL INTESTINAL OBSTRUCTION. DR. T. D. GORDON and DR. A. MORGAN HILL.

The authors record two cases of congenital intestinal obstruction. A review of the subject reveals that congenital intestinal obstruction occurs once in 30,000 births. About 425 cases have been reported. Obstruction was duodenal in 33 per cent of the patients. Causes in the new-born infant are developmental, mechanical or inflammatory. The cardinal signs are persistent vomiting, absence of stools, abdominal distention and visible peristalsis. Roentgenotherapy may be of value. If the condition is recognized before dehydration and intoxication occur, these patients may be benefited by surgical intervention.

DISCUSSION

DR. LEVY: The most important diagnostic point in intestinal obstruction is the vomiting of bile. If the baby vomits bile, the obstruction is below the pylorus; this is how one differentiates the condition from pylorospasm or stenosis.

DR. GORDON: In four cases in the literature operations have been successfully performed. All the patients were operated on early in the disease.

THE EFFECT OF CALCIUM GLUCONATE ON EDEMA IN CHILDREN. DRS. WILLIAM S. O'DONNELL and SAMUEL J. LEVIN.

The mechanism of edema, as it occurs in nephritis and nephrosis, was discussed. Various methods of treatment were mentioned. Three cases of nephrosis were presented, and the effect of calcium gluconate on the edema was shown.

The administration of calcium gluconate parenterally was not accompanied by any undesirable symptoms. The calcium gluconate did not seem to have any harmful effect on the edematous tissues into which it was injected. Ascites, hydrothorax and general edema disappeared rapidly after injections of calcium gluconate. The authors think that the use of calcium gluconate and a diet optimal in protein should prove useful in the treatment of children with nephrosis.

KIDNEY FUNCTION TESTS. DR. F. H. LASHMET.

A kidney function test must satisfy certain requirements. First, as all the glomeruli in the kidney are not ordinarily active simultaneously, in a test of function, the kidneys must be under sufficient strain to insure maximum function. Second, the test must present to the kidneys a definite amount of waste products to be eliminated in a unit of time and in the presence of a minimum amount of water. Third, in an ideal test, one should determine the ability of the kidney to eliminate each one of its excretory products. It is too presumptuous to assume that total kidney function may be determined by the amount of elimination of a single substance, such as urea or a dye, except perhaps in advanced cases. Fourth, the test should be as simple as possible.

Most of the present day tests of kidney function do not satisfy these requirements. A test that fulfils these requirements and that was devised by the author is made as follows: The patient is put at rest in bed on a definite diet, with 1,500 cc. of fluid daily for a period of three days. At 6:00 p. m. of the third day all intake, both of food and of fluid, is stopped until noon the following day. The specimen of urine from 10:00 a. m. to noon is obtained, and its specific gravity carefully determined by the pyknometer.

In twenty-five normal patients the specific gravity was 1.026 or above. In ninety-five patients in whom there was clinical evidence of damage to the kidneys, all but four failed to reach 1.026. In these four there was essential hypertension, and the high specific gravity was presumably evidence of the satisfactory state of the kidneys.

In comparison, this test conformed to the clinical findings in 36 per cent more cases than the phenolsulphonphthalein test and in 73 per cent more cases than the nonprotein nitrogen test of the blood.

CYANOSIS. DR. ARTHUR R. TURNER.

A review of some of the literature on cyanosis was presented. The causes and mechanism of cyanosis and some clinical conditions associated with it were clearly discussed.

CHOREA MINOR. DR. R. W. WAGGONER.

The author believed that infections, such as acute rheumatic fever, acute tonsillitis, acute nephritis, scarlet fever, etc., are coincident or precipitating factors and not the primary causes of Sydenham's chorea. Absolute mental and physical rest and removal of foci of infection were the therapeutic measures advised.

LIPOIDAL SUBSTANCES AS ANTIGENS. DR. WILLIAM W. REDFERN.

It has generally come to be considered that only protein substances are capable of antigenic action. Certain investigators have shown lipoidal fractions of the heterophile antigen to be antigenic if mixed with human serum in vitro before injection. Perhaps the lipoidal fraction of certain nonantigenic organisms (such as the gonococcus) can be combined with a strongly antigenic protein in such a way as to stimulate production of antibodies against the nonantigenic group.

The serum of rabbits that had been given three doses of whole human serum was used in the experiment as the antiserum. The lipoidal extract of the antigen was obtained from normal human serum by extraction, and caprylic alcohol was used as the final solvent. Precipitin tests were performed, and mildly positive reactions were obtained, suggesting that the reactive property of antigen in human serum is present in its lipoidal fraction.

Lipoid extracts of human serum, mixed with horse serum and injected into rabbits, failed to produce antihuman precipitin. The author pointed out that this was a preliminary report and that further work was necessary to confirm the experiments.

THE B C G. DR. DANIEL BUDSON.

B C G is a vaccine of avirulent, living tubercle bacilli. Originally it was a virulent bovine tubercle bacillus, isolated in 1906 by Calmette and Guérin. It was cultivated over a period of thirteen years, in identical conditions. It has lost its virulence for all of the laboratory animals. It has retained intact its antigenic properties. In 1921, B C G was first used in vaccinating new-born infants of tuberculous mothers.

The vaccine is given orally during the first ten days of life, at two day intervals, for three doses. Later in life it can be given subcutaneously, though in smaller doses. Only one inoculation is necessary. In France alone over 258,000 vaccinations were done.

This vaccine confers immunity to tuberculosis. The immunity lasts probably two years. The vaccine is apparently harmless. No untoward reactions occur, except for an occasional cold abscess at the site of inoculation. The reaction to Pirquet's test becomes positive in from six to eight weeks. The author believed that the objections raised against the use of the vaccine did not seem valid.

THE AGGLUTINATION REACTION. DR. M. H. SOULE.

The serum of an animal immunized against one micro-organism often agglutinates other closely related species. The titer of the serum for the homologous organism is usually greater than that for the heterologous germ, and the terms major and minor agglutinins have come into use. In general, the specificity of a protein as antigen is determined by one special chemical group. As an example, it is known that the polysaccharide from type I pneumococcus, coupled with various proteins and injected into animals, engenders type I specific antiserum in every case.

It is generally recognized that one organism may give rise to more than one type of colony. As an example, B. typhosus usually gives rise to a smooth (S) form of colony, but occasionally a rough (R) form is produced. When S organisms are used to immunize animals, S and R agglutinins are produced. When R or heated S bacteria are used, only R agglutinins are produced. Other types of colonies with a number of distinct agglutinogens occasionally develop, and complications are introduced by the fact that in ordinary cultures used as antigens the various agglutinogens may be present in varying proportions. By way of example, it may be stated that fourteen agglutinogens have been demonstrated in cultures of B. paratyphosus.

In general, R agglutinogens are cosmopolitan, the same agglutinogen occurring in widely different genera of bacteria. The agglutination test would therefore be of little value in the diagnosis of infections due to organisms of the R type, but, fortunately, the virulence of the organisms of this type is low.

Persons who have had typhoid fever but whose blood no longer contains many agglutinins may show a high content of typhoid agglutinin when infected by some other organism or after any febrile attack. It is believed that, like other antibodies, agglutinins are probably preexisting substances enormously increased in amount or mobilized following stimulation by foreign proteins.

The unfortunate modern trend is to consider every incidence of an obscure fever that gives a positive agglutination test for B. abortus, in titer as low as 1 : 10, to be undulant fever. In cases in which the serologic observations are not in agreement with the clinical picture, the agglutination test should be augmented by cultural studies. The limitations of such an important serologic test as the agglutination reaction should always be recognized by the clinician.

CIRCULATORY FAILURE IN DIPHTHERIA. DR. JOHN E. GORDON.

Circulatory failure in the acute stage of diphtheria differs distinctly from the similar condition that develops during convalescence. The pathogenesis of these two forms of cardiac involvement is of different nature. The indications for treatment are distinct.

Early circulatory failure is a part of the general intoxication of acute diphtheria. It may develop from the second to the ninth day of the disease. The temperature is usually elevated, the pulse rate is rapid, the heart sounds are well heard, and no disturbances in cardiac rhythm are distinguished, except as a terminal event. The blood pressure is normal.

In early circulatory failure there is probably a disturbance in carbohydrate metabolism, as evidenced by glycosuria and hypoglycemia. This would seem to indicate the use of dextrose and insulin in treatment. Furthermore, Edmunds has shown that improved tone is conferred on the muscles of the heart by the use of dextrose in diphtheritic intoxication of experimental animals.

For the past two years, a 10 per cent solution of dextrose administered intravenously, covered by insulin, has been used in the management of patients with massive infections, when circulatory failure was apparent or anticipated. The procedure has given improved results, not only in early circulatory failure but also in late failure, by an apparent decrease in the frequency with which it is likely to occur.

Late circulatory failure may occur on from the seventh to the thirtieth day, but most commonly on from the twelfth to the fourteenth day. The temperature is normal or subnormal; vomiting is a regular symptom. There is abdominal pain, and the liver is enlarged. The heart is commonly enlarged; there are bradycardia, indistinct heart sounds, arrhythmia and progressive and marked hypotension.

In late circulatory failure there is undoubtedly myocardial damage, but experimental evidence points to the primary source of the trouble in the peripheral vasomotor mechanism. It is thought that the trouble is with the receptive substance, the myoneural junction. Edmunds believes that the toxin unites with the receptive substance, resulting in loss of control of the abdominal blood vessels. With relaxation there is a drop in blood pressure.

Ordinary stimulants have no effect on late circulatory failure. Digitalis is contraindicated. Pitressin, or betahypophamine, has been used with encouraging results. Two precautions must be taken in its use. First, the intake of fluids must be relatively large, not only to aid in blood pressure, but because definite reactions may otherwise follow subcutaneous injections, blanching of the skin, pallor of the mucous membranes and emesis. A second consideration is effective control by frequent determination of the blood pressure. Pitressin is given subcutaneously in doses of from 0.25 to 1 cc. at twelve hour intervals until the desired effect on the blood pressure is obained. Results have been significant and encouraging.

THE EFFECT OF VIOSTEROL ON RACHITIC RATS (Preliminary Report). DR. A. D. EMMETT, KATHARINE M. JARVIS, D. MURRAY COWIE.

The basic object of the study was to ascertain how viosterol would react on rachitic white rats over a long period of treatment, while the rats were still on the rachitic diet.

Two kinds of crystalline viosterol were employed, one from yeast fat and the other from ergot fat.

Rickets developed in each case at about the same rate, regardless of the type of diet. The diets used were McCollum ration 3143 and the Steenbock ration 2965. The rate of healing, as shown by roentgenograms, varied with the increase of the minimum dosages. The time of healing was not accelerated in proportion to the amount of viosterol. The tendency was not to go beyond the approximate level of the average larger dose.

No hypercalcemia was manifested even with excessive doses of viosterol. The phosphorus in the blood increased to normal with treatment. There seemed to be no differences in the influence of diet, of amount of viosterol or of kind of viosterol on the phosphorus in the blood. There was no indication of deposits of calcium or hypercalcemia of the heart, aorta, spleen, stomach and lungs. The liver showed slight fatty degenerative infiltration, and in three or four cases small areas of

moderate calcification. The kidneys showed cloudy swelling of the tubules and some sclerosis, or slight calcification.

These data indicate that there were no toxic effects produced in the white rats kept on the rachitic diets and given viosterol-100 D from either ergot or yeast fat, even when the treatment consisted of large doses and was carried out over a long period.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

JOHN CAFFEY, M.D., *Secretary*

Jan. 14, 1932

HERBERT B. WILCOX, M.D., *Chairman*

SYMPOSIUM BY MEMBERS OF THE DEPARTMENT OF PEDIATRICS, JOHNS HOPKINS MEDICAL SCHOOL

I. THE EFFECT OF COPPER ON IRON METABOLISM. HUGH W. JOSEPHS, M.D.
DISCUSSION. RANDOLPH WEST, M.D.

II. THE PROGNOSIS OF NEPHRITIS AND NEPHROSIS IN CHILDREN. HARRIET G. GUILD, M.D., and VIVIAN TAPPAN, M.D.
DISCUSSION. JOHN D. LYTTLE, M.D., and ALEXANDER J. SCHAFFER, M.D.

III. CALCIUM AND PHOSPHORUS STUDIES: VIII. SOME ASPECTS OF MINERAL METABOLISM IN PARATHYROID TETANY. DAVID H. SHELLING, M.D.
DISCUSSION. EDWARDS A. PARK, M.D.

IV. ROCKY MOUNTAIN SPOTTED FEVER AND TICK-BITE FEVER IN CHILDREN. PAUL G. SHIPLEY, M.D.
DISCUSSION. THOMAS M. RIVERS, M.D.

V. STUDIES OF FAT METABOLISM IN INFANTS. L. E. HOLT, JR., M.D., H. C. TIDWELL, M.D., C. M. KIRK, M.D., and M. CROSS, M.D.
DISCUSSION. WARREN M. SPERRY, M.D.

THE EFFECT OF COPPER ON IRON METABOLISM. DR. HUGH W. JOSEPHS.

It is self-evident that when blood destruction exceeds blood formation anemia will develop, and, vice versa, when blood formation predominates the red cells and hemoglobin will rise. The work presented here is an attempt to express quantitatively the relation between blood destruction and blood formation, the urobilin excretion in the stools being used to measure blood destruction and the reticulocyte percentage to measure blood formation. The units in which these two processes have been expressed have been arbitrarily chosen, and are open to obvious criticisms.

It seemed fair to assume that the rate of urobilin excretion would be normally proportional to the total amount of circulating hemoglobin, and the unit of blood destruction used in this work is 0.4 mg. per gram of circulating hemoglobin. The total circulating hemoglobin is obtained from the formula: weight (Kg.) $\times$ 0.76 $\times$ hemoglobin (Gm. per hundred cubic centimeters of blood), assuming that the normal blood volume is 76 cc. per kilogram of body weight. The unit of

blood formation is 0.7 per cent of the reticulocytes. It is evident from the roughness of the measurements involved that exact quantitative relationships cannot be expected.

On application of these units to cases of anemia, it was found that when the units of blood destruction exceeded those of blood formation the red cells and hemoglobin tended to fall, and that when the units of blood formation predominated the red cells and hemoglobin tended to rise. This was clearly shown in a case of pneumonia in which there was a relapse after a week of apparent convalescence. During the acute stage of pneumonia, there was found to be usually a moderate increase in normal urobilin, amounting to four or five units, while the reticulocyte percentage remained low. As soon as convalescence was established, the reticulocyte units predominated. In one or two cases in which there was a failure of the hemoglobin to rise, there was found to be an unexplained transitory rise in the excretion of urobilin to such an extent that the units of urobilin excreted tended to approximate or even to exceed those of the reticulocyte percentage. One case was shown illustrating hypoplastic reaction in pneumonia, and another in which there was a very marked hemolytic reaction with jaundice. In several cases of anemia on a nutritional basis, there was a predominance of blood destruction, for which no explanation was found.

The quantitative expression of the factors of blood formation and destruction has been found of value in the anemias of infants that develop on an infectious or nutritional basis. It has been found of relatively little value in attempting to explain the variations of hemoglobin and red cells in the first months of life in premature babies, or in the types of anemia dependent on profound damage to the hematopoietic tissue, as in some cases of syphilis. It was also found that while the red cells tended to behave as expected, according to the predominance of blood formation or destruction, the hemoglobin might act to a certain extent independently.

DISCUSSION

DR. RANDOLPH WEST: I think that this attempt to measure blood production and destruction quantitatively is most interesting and important. There are a great many assumptions that are necessary in any field as complex as this. In certain types of anemia, it is probably not applicable. In the papers given this evening, it is applicable and gives a satisfactory method of study. In some nutritional anemias, it might be hard to think the reticulocytes an accurate index of blood formation.

The rise in hemoglobin following the administration of copper, even in patients who had an adequate amount of iron, is also interesting, and one is tempted to speculate in this field and to associate the methods applied with their probable point of union in the molecule.

It is of great interest that in a rather different field, the first definite chemical compound, a porphyrin containing both iron and copper in one molecule, has been identified by Dr. Coulter from certain diphtheria cultures that he has been studying. It is quite possible that some similar combination may be necessary as an intermediate product in the complete formation of hemoglobin.

Regarding reticulocytes, it seems that they may be more properly considered as an index of excessively rapid blood formation than as an index to the normal rate of blood formation.

THE PROGNOSIS OF NEPHRITIS AND NEPHROSIS IN CHILDREN. DR. HARRIET G. GUILD and DR. VIVIAN TAPPAN.

ACUTE GLOMERULAR NEPHRITIS.—One hundred and eighty cases of acute glomerular nephritis were on record in the files of the Harriet Lane Home of the Johns Hopkins Hospital up to the spring of 1928. Although twenty-eight of the patients died, only six (3.33 per cent) died of the nephritis itself. The immediate prognosis may, therefore, be regarded as extremely good.

In an effort to determine the ultimate prognosis, whether or not an attack of acute glomerular nephritis led to the development later of chronic nephritis, a follow-up examination was made of as many patients as it was possible to locate for study. Thirty-four patients, who had had acute glomerular nephritis from one to twelve years previously, were examined. Eighteen (group I) were seen less than five years, and sixteen (group II) more than five years, after the nephritis.

All, excepting one girl with advanced rheumatic heart disease, were symptomatically well and leading normal lives.

Nine patients showed albuminuria, four in group I and five in group II. Three of these had only orthostatic albuminuria. Another, with advanced rheumatic heart disease, showed a constant trace of albumin which can be explained on the basis of circulatory insufficiency, as a mild degree of cardiac decompensation is always present. This leaves two in group I and three in group II who showed persistent albuminuria, which, in the absence of other causes, may be attributed to the nephritis. In one of the latter, eleven years had passed since the nephritis.

None of the patients in whom examination was satisfactory showed any impairment of renal function. In all of the patients with albuminuria, the level of function was well above that regarded as the lower limit of normal, while the average for them as a group was as high as that for the patients found to be entirely normal. Furthermore, reexamination of the abnormal group from six months to two years after this first follow-up examination showed no change in the status of the kidneys.

All but six of the patients were 7 years of age or less at the time of their nephritis. The percentage of these patients now showing albuminuria is definitely less than the percentage of those in whom the nephritis occurred at an age beyond 7.

The type of infection preceding the nephritis had little influence on the outcome. One of the four patients in whom it followed scarlet fever was among those found to be abnormal. Also, among the abnormal patients was one who had acute nephritis complicating congenital syphilis at the age of 2 months.

The severity of the nephritis and the duration of the patient's stay in the hospital did not seem to influence the prognosis.

In the majority of the patients who are now normal, the urine cleared quite promptly, in most within two months. In several, however, complete clearing took place even after the albumin had persisted for many months. In fact, one cleared after showing red blood cells in the urine for six months and albumin for as long as one year. These patients have had no recurrence of their trouble.

In twenty patients, foci of infection were not eradicated following the nephritis. Sixteen of these were among the twenty-five patients who are now entirely normal in all respects. Five more of the normal patients had some other focus of infection, at least in the teeth, so that only four were entirely free from any focus. Three of the nine albuminuric patients were without discoverable foci of infection.

Fifteen of the normal patients passed through subsequent infections without a recurrence of nephritis, including one in whom scarlet fever and erysipelas were the infections experienced. The four albuminuric patients in group I had no intercurrent infections.

Only one patient in the entire group had had a real recurrence of nephritis with a subsequent infection, and he is now normal except for an orthostatic albuminuria.

Conclusions.—From this analysis one cannot escape the conclusion that in acute glomerular nephritis in children the ultimate as well as the immediate prognosis is good, and, in general, the younger the child, the better the prospect of complete recovery. Even when the urine fails to clear entirely, albuminuria may persist for years without impairment of general health or renal function. It may also disappear completely after it has been present for at least as long as a year. Children who have once had acute nephritis stand subsequent infections without greater liability to complicating renal disease than children who have never

had nephritis. It seems quite possible that the condition of some who are still showing abnormal urinary constituents may yet clear up entirely, and that those in whom the condition fails to clear up will continue to do well for many years in spite of the albuminuria.

MIXED NEPHRITIS.—Of forty-five patients on record in the Harriet Lane Home who presented the nephrotic syndrome — anasarca over long periods of time and massive albuminuria, usually with reduced blood protein and an inversion of the albumin-globulin ratio — twelve are regarded as having mixed nephritis because of the presence of frank hematuria or persistent microscopic hematuria.

The prognosis in this group was very poor. Nine died within from six months to five and one-half years after the onset of the disease; six died of renal insufficiency (one having survived pneumococcus peritonitis at one stage of the disease); two died of infection (pneumonia in one and pneumococcus peritonitis in the other), and in one the cause of death was unknown. Of the three patients who are living from two months to three years after the onset, two showed signs of progressive renal insufficiency, and one, though well when last seen, excepting for the abnormal urinary constituents, had been under observation for only eight months when he was "lost sight of."

NEPHROSIS.—Thirty-three of the forty-five patients presenting the nephrotic syndrome may be regarded as having a "simple" nephrosis, in the ordinary clinical sense of the word. The prognosis in this group is better than that in the group of mixed nephritis, but not nearly so good as that in the cases of acute glomerular nephritis. Fourteen of the thirty-three patients are dead, most of them having died of infection, most often a pneumococcus infection of which pneumococcus peritonitis was a part. They did not die of renal insufficiency, and death occurred from intercurrent infection anywhere from three weeks to four and one-half years after the onset of the disease.

Of the nineteen survivors, only eight were entirely well, in that there had been complete clearing up of the urine as well as freedom from symptoms. Recovery took place from four and one-half to ten and one-half years after the onset. In eleven the disease was still active from three months to ten and one-half years after the onset: three (after from six months to seven years) were seldom free from edema; two (after six months and seven and one-half years) showed only transient attacks of edema with a persistent albuminuria, and six (after from three months to ten and one-half years) at the time of examination showed only albuminuria as an indication of their disease. It is of interest that in this group of thirty-three patients with nephrosis, seventeen had at some time for a brief period shown a few red blood cells in the urine on microscopic examination. This includes two of those who were entirely well. The clinical course had otherwise been so typically that of "simple" nephrosis that the appearance of just a few transient red blood cells in the urine was not regarded as inconsistent with a diagnosis of nephrosis. It is only when hematuria had been grossly or persistently present that the cases were relegated to the group of mixed nephritis.

The frequency of the occurrence of pneumococcus peritonitis in this group also bears emphasis. It occurred in eleven, or just one third, of the cases. Although some survived one or even more (up to four) attacks, the pneumococcus peritonitis was the terminal event or part of a terminal generalized pneumococcus infection in seven of the cases.

In this group, then, the danger is not from progressive renal insufficiency with death in uremia, but from the development of intercurrent infection during a period when the patient is suffering from active symptoms of the disease, though still possessing good renal function. If, on the other hand, the patient survives or escapes these intercurrent infections, his chance of complete recovery is fairly good, although it is a matter of years (four and one-half years is the shortest duration in this group) rather than of weeks, as in the usual case of acute glomerular nephritis, before such recovery takes place.

DISCUSSION

DR. JOHN D. LYTTLE: It is always interesting to see the material from another clinic, and I am sure that we are very much indebted to Dr. Guild and Dr. Tappan for the interesting and instructive analysis of the cases from their clinic.

I hesitate to show our figures here, because it seems to me it is much better to have nephritis or nephrosis in Baltimore than in New York. Our series of nephrosis at the Babies' Hospital is not so large and has been observed for only two and one-half years. In fifteen cases, glomerular nephritis has developed in two patients, four are still active, three are cured, and six, or 40 per cent, have died. Since it is difficult to estimate a cure at one or two years, these figures may change. I have been interested in the sex of the patients in this type of nephritis. In the series observed at Bellevue Hospital, 100 per cent were males. In this group, 77 per cent are males, and of the six patients who died, five were males. Of the three called cured, two are females. Except for statistics, I think we have very little evidence on which to base the prognosis of nephrosis.

We have been able to follow thirty-nine cases of glomerular nephritis from six months to two and one-half years. The immediate prognosis is good; only two of this group died during the acute attack. The cause of death in one case was cerebral edema, and in the other acute cardiac failure with terminal sepsis. Chronic nephritis developed in fifteen, or 38.5 per cent, of the patients. While renal function and the degree of renal damage in these cases is variable, they all have definite clinical and urinary signs of chronic nephritis. Five patients died in uremia, which brings the total mortality to 18 per cent.

To date, we have called twenty-two, or 56.4 per cent, of the patients cured. This percentage also may change with time. The great difference in the figures shown by Dr. Guild is interesting. I believe that the age level of Dr. Guild's patients is lower than mine. In the group of patients called cured, the average age is 4 years, and only 18 per cent are 7 years or older. In the group in which the disease became chronic, the average age is 8 years, and 66 per cent are 7 years or over. I hesitate to say that all of the children with chronic nephritis are headed for uremia, but there are very few cases on record in which the nephritis has been active for a year or more that have gone on to a cure.

In attempting to make a prognosis in glomerular nephritis, there are three important points to be considered: The first is the persistence of albuminuria. The nephritis continues with varying degrees of activity, and if the patients are followed carefully, it is found that they have never recovered from an attack of acute nephritis. The second point is the constitutional factor in nephritis. Seven, or 46 per cent, of cases of chronic nephritis have a family history of cardiac disease, nephritis or hypertension. In the cured group, only four, or 18 per cent, have a positive family history. I feel that this is a significant difference. Shick quotes Spieler somewhat as follows: "There are 83 families with 186 children simultaneously sick with scarlet fever. In 48 families with 103 children, there was no nephritis, while in 35 families with 83 infected children, 51 children had nephritis." Of course one must take environment into consideration, but it seems to me this evidence is suggestive of a "familial disposition." The third point is the relation of hemolytic streptococcus to glomerular nephritis. It is quite true, as Addis says, that "we cannot write hemolytic streptococcus plus the patient equals nephritis," yet, if the urine is examined carefully following streptococcal infection, it will be found that it shows some evidence of renal irritation in the postfebrile period, i. e., at the time one looks for the development of nephritis in scarlet fever.

The reactivity of the skin to the products of hemolytic streptococcus does not give any reliable information. The tests are just as often positive in cases in which the disease is called cured as in the cases that have become chronic.

Recurrence or persistence of infection has been observed in cases of chronic nephritis. For example, acute glomerular nephritis develops in a 5 year old boy with an abscess of the lung associated with hemolytic streptococcus. In two months, the nephritis is called cured, and he is followed closely for over a year

without any signs of nephritis appearing. The condition in the lung continues; he has several attacks of infection of the upper respiratory tract associated with hemolytic streptococcus. His tonsils are removed, and an abscess is found at the bottom of one tonsil, with hemolytic streptococcus on culture. During all these incidents, the urine is clear, except for slight changes during a febrile period, but there is no evidence of nephritis. Glomerular nephritis develops in another child of the same age following otitis. Chronic mastoid disease and chronic sinusitis associated with hemolytic streptococcus develop. This child never recovers from the acute glomerular nephritis. The first child is able to make a successful fight against the hemolytic streptococcus, while the second child is unable to. When the constitutional and immunologic differences between such children are known, one will be in a better position to predict results instead of merely following the course of glomerular nephritis.

DR. ALEXANDER J. SCHAFFER: The remarks I was going to make concerning Dr. Guild's paper were thrown completely out of kilter by Dr. Lyttle's statistics. I wonder whether this difference in their figures represents a geographic distinction, such as a difference that was called to mind by Dr. Guild's figures on nephrosis. She quoted, as you will recall, a high incidence of intercurrent infections in her series, practically all caused by the pneumococcus; if I correctly remember Dr. Blackfan's series, published several years ago, almost all of the intercurrent infections occurring in his Boston patients seemed to be caused by a streptococcus, whereas, in New Haven, geographically between Baltimore and Boston, the organisms causing complications are about half streptococci and half pneumococci! Be that as it may, it is quite certain that all of us who have been at the Harriet Lane Home have received the decided impression that acute nephritis in children is a mild disease. I remember having a discussion with a pathologist and an internist on one occasion because the pathologist remarked, and the internist agreed, that one of the diseases he would prefer to avoid above almost all others was acute hemorrhagic nephritis. It was their impression, derived chiefly from observation of adults, that a great many acute cases become subacute or chronic; mine, derived entirely from children, was that if the patients recover from the acute attack, they remain completely well thereafter. Shortly afterward, the paper of Van Slyke and his co-workers appeared, and my friends felt vindicated; at about the same time Dr. Guild's figures began to take shape, and I felt vindicated. It seemed then that the answer was that the prognosis for adults is bad, but that for children is good; now, however, that I have heard Dr. Lyttle's statistics, I am afraid there is no answer quite so simple as that.

CALCIUM AND PHOSPHORUS STUDIES: VIII. SOME ASPECTS OF MINERAL METABOLISM IN PARATHYROID TETANY. DR. DAVID H. SHELLING.

In the course of study on the effect of dietary calcium and phosphorus on the metabolism of these elements in parathyroidectomized rats, it was noted that the intake of phosphorus plays a determining note in the provocation of tetanic symptoms, hypercalcemia and anorexia. Thus, the animals could be made tetanic by diets either optimal in phosphorus but low in calcium or optimal in calcium but excessive in phosphorus, and the tetanic symptoms could be alleviated either by the addition of calcium or by the reduction of phosphorus in the rations. The diets most efficacious in giving relief from tetany were those in which phosphorus was low and the calcium optimal or high. Analysis of the urinary and fecal excretion of these elements on the various diets before and after parathyroidectomy revealed that on tetany-inducing diets, the animals operated on retained phosphorus and were unable to excrete the excess in the urine. The retention, however, could be overcome by the addition of cations, such as calcium magnesium and strontium, which are capable of forming insoluble salts with phosphorus in the intestines and thus remove the retained phosphorus from the body. The reduction of the serum inorganic phosphorus by its excretion into the bowel allowed a rise in the serum calcium concentration and a relief from the tetany. When, however,

the intake of phosphorus was excessive, the tetanic symptoms frequently continued and the serum calcium remained at low levels, in spite of an increased intake of calcium.

The same metabolic disturbance was found to be operative in a patient suffering from parathyroid tetany. A case was studied with Dr. Reed Ellsworth. When the patient was admitted to the hospital with active tetany, the calcium was 5.8 mg. and the phosphorus 6.5 mg. per hundred cubic centimeters of blood, in spite of a daily intake of 2 Gm. of calcium (in food and calcium lactate). On this dietary regimen, the levels of calcium and phosphorus in the blood remained about the same, and the patient exhibited tetanic manifestations. On the fourteenth day, the dietary phosphorus was reduced to one-fourth, but the calcium was kept at the 2 Gm. level. On this ration, the serum phosphorus decreased, the calcium rose gradually, and the patient was free from active tetany, although the Trousseau sign could still be obtained in from three to five minutes, instead of from twenty to thirty seconds, as previously.

When viosterol was added to the diet for four days, there was a rise in both the serum calcium and phosphorus. When it was discontinued, the calcium level in the serum dropped first and the phosphorus remained high; and on the fifth day after discontinuing the administration of viosterol violent tetany developed from which the patient was relieved by rebreathing. Magnesium (0.85 Gm. daily as $MgCO_3$ [magnesium carbonate]) was next given. The symptoms of tetany disappeared promptly in spite of a relatively high phosphorus and low calcium level in the blood.

In order to show that viosterol and parathyroid extract-Collip do not act alike in relieving patients from parathyroid tetany, 100 units of the extract were administered to the patient and frequent determinations of the serum calcium and phosphorus were made for a period of twenty-four hours. It was found that, in contrast to viosterol which invokes a rise in both calcium and phosphorus, the parathyroid extract produced an abrupt fall in the serum phosphorus, and the rise in calcium occurred only after twenty-four hours.

Analysis of urinary calcium and phosphorus in this patient showed changes analogous to those found in the parathyroidectomized rats. During the stages of active tetany and retention of phosphorus in the blood, the urine contained moderate amounts of phosphorus but either little or no calcium, and during the tetany-free periods, the retained phosphorus was excreted in the feces, and the urine was free from this element. During the viosterol-feeding period, the retention of phosphorus in the blood was reflected by the presence of moderate amounts in the urine, but during the period of administration of the parathyroid extract, the urinary excretion of phosphorus in twenty-four hours was enormously increased, the patient excreting, in the urine alone, nearly 1 Gm. of phosphorus on a 0.25 Gm. intake.

A second patient with parathyroid tetany is being treated at present with similar dietary regulations, i. e., with a low phosphorus ration in which the amount of calcium (or calcium plus magnesium) is about four times that of phosphorus.

DISCUSSION

DR. E. A. PARK: Dr. Shelling's work is most interesting. The experiments which he has described tonight are parts of an extended series. They point to a particular relationship between parathyroid function and phosphorus metabolism, a relationship to which Dr. Greenwald especially has already directed attention. This relationship is most important both from the theoretical and practical points of view and is not sufficiently appreciated. In parathyroid tetany the thought has always been concentrated on the calcium. But the complete intolerance of the animal to phosphorus is as striking and fully as important a phenomenon as the low level of the serum calcium, as Dr. Shelling's experiments so excellently show.

When Dr. Shelling and I called on Dr. McCollum in order to obtain his opinion as to why Dr. Shelling's parathyroidectomized animals failed to take the diet when the phosphorus was high, Dr. McCollum made the remark that either the

animals did take the diet and were made sick by it, so that before long they refused to take it entirely, or else there was a spirit inside the animal that whispered that the diet was bad for him. Dr. Shelling was at first inclined to think that a spirit from within whispered to the animal to abstain, but, when he observed the animals carefully, he discovered that they from time to time sampled the diet, taking minute quantities, and determined apparently by a process of trial and error whether to take more or to leave it alone. Finally, when convinced by digestive experience that the new diet, low in phosphorus, was good, they rushed at it and gorged. I wonder if human beings are not guided in their selection of food in exactly the same manner as Dr. Shelling's rats, the children of Dr. Davis' study in Chicago, for example. A given child keeps eating a food, A, until he becomes sated, i. e., is on the verge of being sick. He then loses his appetite for A and proceeds to test out other foods, e. g., B and C. Finding himself favorably affected by B and C, he continues to eat them and will continue to eat them indefinitely so long as his well-being remains entirely unaffected, but as soon as it is affected, he begins a search elsewhere, trying other foods. Such an hypothesis presupposes not only that the loss of appetite is specific for a certain food or group of food substances, but that an appetite for other food substances is retained. Otherwise, the animal or child would stop eating altogether and would not continue to search for new foods. Livingston in his African travels described the hunger for salt that he experienced after prolonged deprivation, and how salty milk and meat tasted, when finally he once secured them. If an animal or human being has specific losses of appetite, it seems probable that at the same time particular cravings develop and that his trials of new foods are the results of protective appetites developing in new directions. But the factor determining the appetite or loss of appetite for a given food must be whether or not the food maintains a state of euphoria.

The experiments of Dr. Shelling, as he has indicated, have an important practical value in showing that in the treatment of tetany, particularly parathyroprival tetany, the diet ought to be high in calcium but at the same time low in phosphorus. But, of course, it is difficult to devise a diet low in phosphorus, though easy to make one high in calcium. However, the high calcium, as Dr. Shelling has shown by experiment, aids the patient to get rid of the phosphorus through the excretion of the latter from the bowel.

ROCKY MOUNTAIN SPOTTED FEVER AND TICK-BITE FEVER IN CHILDREN. DR. P. G. SHIPLEY.

The typhus-like fevers of the United States may be classified as follows: (1) epidemic (European) typhus fever; (2) Brill's disease; (3) endemic (American) typhus, and (4) tick-bite fever, (*a*) Rocky Mountain spotted fever, and (*b*) tick-bite fever of the Atlantic Coast.

The two types of tick-bite fever are identical immunologically, but differ in mortality rates and in the behavior of the causative virus toward laboratory animals.

In the southern states on the Atlantic Coast, typhus and tick-bite fever exist side by side. The first is a winter and an urban disease. The second is a malady affecting rural districts in the spring and summer. All ages and both sexes are attacked. In Maryland, the bayside counties are chiefly affected. The morbidity is increasing; the mortality is about 20 per cent.

Tick-bite fever in Maryland is transmitted by the wood or dog tick, Dermacentorvariabilis and perhaps by other ticks, during the act of biting. It has been acquired, probably through minute abrasions, by crushing infected ticks between the fingers. The seasonal incidence of ticks and tick-bite fever is coincident, from March to September.

The virus is probably represented by Rickettsiae, which may be recovered in small numbers from the tunica vaginalis testis of guinea-pigs which have been inoculated with the *materies morbi* of the disease. The Rickettsiae may be found

in large numbers in films made from scrapings of the inner surface of the corneas of guinea-pigs suffering from the specific kerato-uveitis that follows injection of morbific material into the anterior chamber of the eye. Guinea-pigs and rabbits are easily infected by the injection of blood or emulsions of spleen of infected animals or of blood from patients with the disease. The infection is rarely fatal to animals. An inflammation of the scrotum usually develops in the infected guinea-pig which does not become gangrenous as does the scrotal lesion seen in guinea-pigs with Rocky Mountain spotted fever. The virus also does not cause gangrene of the ears of infected rabbits. The animals have fever that may be of the saddle-back type. The blood of infected guinea-pigs is not infectious after the sixteenth day of the disease. Infection with tick-bite fever of the coast protects animals from Rocky Mountain fever and vice versa, but affords no protection against the virus of typhus. The virus is probably a variant strain of the virus of the Rocky Mountain disease.

The characteristic lesions of the disease are enlargement of the spleen and enlargement of, and hemorrhage into, the lymph nodes.

In children, the period of incubation is short. The extremes so far seen are from two to ten days. The onset occurs with fever, drowsiness and, frequently, severe frontal headache. Occasionally, backache or pain in the joints may be complained of. There may be vomiting.

Both mild and severe infections are seen in children, but all grades of severity between the extremes exist. In severe infections, apathy becomes stupor with nocturnal delirium. The pyrexia is continuous and high (between 40 and 41 C. [104 and 105.8 F.]) with a tendency to remission about the seventh day. The disease terminates usually by a fairly rapid lysis. These patients are covered with the eruption and resemble patients with severe cases of epidemic typhus. Patients with mild cases are apathetic only for a day or two. They maintain a temperature for from eight to ten days of 38 to 39 C. (100.4 to 102.2 F.) which then subsides. In them, the eruption is represented by a few macules resembling rose spots. There may be a form *sine eruptione*.

The eruption appears on from the third to the fifth day on the extremities and spreads centripetally. It involves the palms and soles and is thickest on the extensor surfaces, on areas subject to pressure and about the joints. The abdomen is relatively spared, as is the face. At first, the rash is macular and rose colored, but as the disease progresses, it becomes papular and hemorrhagic. It persists after defervescence and is followed by a branny desquamation. The palms and soles may peel. There is also a subcuticular mottling of the skin. An equivalent enanthema is present.

The pulse is rapid, and the P-R interval may be prolonged. Transient pains in muscles and joints may be complained of, and bronchitis is common. Fifty per cent of our patients showed traces of albumin in the urine. There may be leukopenia or leukocytosis, or the white cells may vary in number from day to day. Cultures of the blood are sterile. The spinal fluid may show an increase in the globulin and a slight increase in the number of cells. B. proteus X-19 and X-2 are agglutinated by the blood serum. The Widal reaction is not given, but non-syphilitic children may have a positive Wassermann reaction during the course of the malady.

There is no specific treatment. The prognosis is good *quo ad vitam* in children, but becomes progressively more unfavorable as age advances. I have seen no sequelae.

DISCUSSION

DR. THOMAS M. RIVERS: I have had no experience with Rocky Mountain spotted fever in children, and hence am unqualified to discuss the clinical aspects of the disease. I shall make a few general remarks about the group of diseases to which this malady belongs. There are five types of disease that have been placed in the Rickettsia group, namely, typhus fever, Rocky Mountain spotted fever, trench fever, flood fever and heartwater disease of sheep. Rickettsiae probably cause all these diseases. Bacillary or coccoid forms of the organisms are found

both in the natural and in the experimental diseases. They appear to be organisms and probably are, but they have never been cultivated in the absence of living susceptible host cells. What kind of organisms are they? Are they ordinary bacilli or do they represent some other form of parasitic life? Work attempting to answer these questions is now in progress in various parts of the world. Some workers contend that the Rickettsiae are small, noncultivatable forms in the life cycle of the proteus bacilli. Felix, for instance, is quite in accord with such an idea. Most investigators, however, are of the opinion that Rickettsiae are not genetically related to proteus bacilli.

I should like to emphasize several interesting facts mentioned by Dr. Shipley. The first is the difference in the distribution of the rash in Rocky Mountain spotted fever and in typhus fever. In the former it appears particularly on the extremities, while in the latter it is most marked on the trunk. The etiologic agent in each instance is carried to the skin by way of the blood. Why is it that in certain closely allied infections the rash is characteristically located on the skin of different parts of the body? The answer to this question may be of interest and importance.

Another point of interest is the prognosis of the disease in children. Dr. Shipley states that children are less likely to die of Rocky Mountain spotted fever than are adults. This is also true of typhus fever, yellow fever and psittacosis. Children have these diseases; they may not be very sick, and the mortality is lower than it is among adults. It would be interesting to know why children are more resistant to these maladies than are adults.

STUDIES IN FAT METABOLISM IN INFANTS. DR. L. E. HOLT, JR., DR. H. C. TIDWELL, DR. C. M. KIRK and DR. D. M. CROSS.

Metabolism studies have been carried out in a series of normal infants in an attempt to evaluate the factors responsible for differences in the absorption of fat. It was found that the size of the fat globules was without influence on the absorption of fat. Retention was quite as satisfactory when butter was fed by spoon, as in experiments in which cow's milk and homogeneized cow's milk was used.

In order to find out whether the somewhat lower fat retention of cow's milk as compared with breast milk was due to differences in mineral content or to differences in the fat itself, these factors were varied independently. The effect of mineral was evaluated by employing cow's milk fat incorporated in (1) skimmed breast milk, (2) skimmed cow's milk and (3) skimmed cow's milk to which additional mineral had been added, approximately doubling the quantity. The following retention figures represent averages for such experiments:

Cow's milk fat + skimmed breast milk, 95.5 per cent retained.

Cow's milk fat + skimmed cow's milk, 86.7 per cent retained.

Cow's milk fat + double ash skimmed cow's milk, 81.4 per cent retained.

Apparently the chief reason for the lower retention of fat on cow's milk as compared with breast milk is the higher ash content of the latter.

However, differences in retention were observed when the only factor varied was the fat itself. In a series of experiments in which skimmed cow's milk was used as a basal diet and various fats were added to this the figures for retention summarized in the accompanying table were obtained:

Retention of Fat on Various Diets

Fat Fed	Iodine Value	Average Retention, Per Cent
Corn oil and olive oil	90–120	92.8
Breast milk fat	56	89.9
Cow's milk fat	26	86.7
Tri-palmitin + tri-stearin	2	61.4

It would thus appear that more highly unsaturated fats are better absorbed than saturated fats.

By determinations of the iodine value and thiocyanogen value of the food fat and fecal fat, we have been able to calculate the retention of the various fractions in any mixed fat. Evidence has been obtained which suggests that when fat mixtures are fed there is a selective absorption of unsaturated fats.

DISCUSSION

DR. W. M. SPERRY: I wish first to congratulate Dr. Holt and his co-workers on this important and difficult piece of work. Any one who has tried to make fat balances on children will know what I mean when I say difficult. There is so much material of interest in this paper that might serve as a starting point for discussion that I scarcely know where to begin. I shall limit myself largely to that phase of the work with which I am most familiar, namely, the excretion of fat. Dr. Holt's metabolism results depended on measurements of the excretion of fat; so, first I should like to say a word about procedures for the determination of fat in the feces. Generally speaking, three such procedures are available. According to the first of these, fat is measured in a single specimen or perhaps in a number of specimens of feces not previously dried. The results are expressed in percentage of fat in the total weight of moist feces. According to the second of these procedures, fat is determined as before in a single specimen or in several specimens of feces that have previously been dried; so the results may be expressed in percentage of fat in the dried material of the stools. The third procedure is the one that Dr. Holt has used in the present investigation, and involves a measurement of the total intake and output of fat over a considerable period of time. In my opinion, results obtained by the first procedure are of very little value because of the wide variation in the water content of the feces and the considerable variation both in the dried fecal material and in the excretion of fat itself. Results obtained by the second procedure, which is the most widely used, are also open to a good deal of question. Holt, Courtney and Fales have made the most extensive series of studies of the excretion of fat in infants and children with which I am familiar. Using the second of these procedures, they found in normal infants on a diet of cow's milk, values for the percentage of fat in dried feces varying from 15.7 to 56.7, while the excretion was found to be within normal limits by the third procedure. In a series of determinations in infants with diarrhea fed a diet of cow's milk, the excretion of fat was found to be high by the third procedure. Nevertheless, in the same persons the percentage of fat in the dried feces determined by the second procedure mentioned varied from 3.9 to 61.4. The average of the last mentioned determinations was 35.1 per cent as compared with 36.2 per cent in the normal subjects. Obviously, the second procedure, i. e., the determination of percentage of fat in the dried stool, showed no differences in these series despite the fact that excretion was abnormally high in one of the groups. In older children fed a mixed diet, the second procedure was somewhat better. The fat, expressed in terms of dried fecal weight, averaged higher in a series of children in which the excretion of fat was shown to be abnormally high by the third procedure, than it averaged in another series in which the excretion of fat was normal. Nevertheless, there was a considerable overlapping of the values obtained in the two groups. The point I want to make is that any determinations of fat based on the dried weight of feces must be interpreted very carefully indeed. It is unfortunate that the only procedure that gives results of unquestioned value is so difficult and time-consuming that it is out of the question for the ordinary laboratory, involving as it does quantitative measurement of the entire intake of food, the fat content of the food, the entire fecal output and its fat content over a period that should not be less than five days and should, preferably, be a week or more. I was very glad to note that Dr. Holt had employed the fat balance method in the work that he has reported tonight.

It is generally assumed, as Dr. Holt has assumed in his experiments, that excreted fat represents unabsorbed food fat, and the absorption of fat is taken as

the difference between fat in the diet and fat in the feces. Evidence has been accumulating, however, for a long time, indicating that there may be an endogenous excretion of fat independent of the diet. I have studied this question in dogs and have shown to my own satisfaction that such an excretion actually exists. It is not particularly large, but continues with little diminution for at least from five to six weeks in dogs that receive no fat in the diet. Variations are large from dog to dog and in the same dog from week to week. The excretion averages from 240 to 250 mg. of fatty substances per week. The question arises whether the excretion of fat measured in infants and children contains an appreciable amount of such an endogenous excretion. I have calculated roughly from the work of Holt, Courtney and Fales that the average excretion per kilogram of weight per week of normal infants on breast milk was 1,820 mg., while the average excretion of normal infants on cow's milk was practically the same (1,786 mg.). From these values I calculated that, if the endogenous excretion in infants is the same as that in dogs, then it would make up only 13 per cent of the amounts found by Holt, Courtney and Fales. If this is true, calculations of absorption, considering that excreted fat represents unabsorbed food fat, would involve only a small error. However, there is some evidence indicating that endogenous excretion of fat may be of greater importance in infants than this calculation shows. Holt, Courtney and Fales found no direct relationship between the amount of fat in the diet and the amount excreted. They performed three interesting experiments. Let me give you the results of one of them. They fed an infant fat at a rate of 38 Gm. per day, and found an excretion of 1.33 Gm. per day in the feces. Then the intake was cut to 5 Gm. per day, but the excretion fell only to 1.11 Gm., and in another period during which the intake was 5 Gm., the excretion was 0.98 Gm. When the intake was increased to 50 Gm. per day, the excretion increased only to 1.78 Gm. Obviously, changes in the excretion were very small when compared with the large changes in the intake. The other two experiments gave comparable results. Again, Hutchinson in a similar series of experiments found no relationship between the intake and the excretion of fat, though he did find some relationship between the excretion of fat and the amount of dried material in the feces. In view of the foregoing considerations, I was extremely interested in one point in Dr. Holt's paper, namely, the experiments with a fat-free diet in infants. From his average results I calculated that he obtained an excretion of 510 mg. per kilogram per week, which may be compared with the average excretion of 250 mg. by dogs. It must be remembered that Dr. Holt's diet was not strictly fat-free, whereas the dogs received no fat at all. These results indicate that the endogenous excretion in infants per kilogram of body weight is somewhat larger than that in dogs, though still not large enough to be of great importance in determinations of fat balance. One is left just about where one was before, with the probability that the larger part of fecal fat is unabsorbed food fat. If this is so, one wonders what the explanation for the excretion is. As far as it is understood, digestion is a very efficient process. Why should moderately large portions of dietary fat escape absorption? There are several possibilities; first, selective absorption. In a review published several years ago, Dr. Bloor was able to find no evidence for such a process. The results obtained by Dr. Holt in this regard are interesting, though I feel that further experimentation is necessary before one can be certain that selective absorption does take place. Another possibility is that fat may be carried out as insoluble soaps. Dr. Holt has presented data that support this as a possible explanation of a portion of the excretion. Another possibility, which was proposed by Hutchinson, is that some fat may be necessary for lubricating the intestinal tract. He explained his finding of a relationship between the amount of fat in the feces and the amount of dried material on some such basis. Dr. Holt thought I might have some explanation for the apparent relationship between unsaponifiable excretion and the amount of ash in the diet. I am sorry to say that I have no explanation. I might say a great deal more about unsaponifiable excretion, but time is not available. I should like to raise just one point in criticism. The

results that Dr. Holt gave us concerning the effect of iodine number on the absorption of fat are interesting and important. I noted, however, that in some of his groups he had only one, two or three cases. In view of the rather large variations in the excretion of fat by normal persons, I wish that these groups had been somewhat larger, and I am sure that as he continues his experiments more such cases will be added.

NORTH PACIFIC PEDIATRIC SOCIETY

L. HOWARD SMITH, M.D., *Secretary*

Twenty-Fifth Semi-Annual Session, Jan. 23, 1932

A. HOWARD SPOHN, M.D., *President, in the Chair*

DIABETES. DR. FRANK DOUGLAS, Seattle.

A boy, aged 7 years, presented a condition which had been diagnosed as diabetes over one year previous to presentation. During eleven months before his last illness, however, the patient remained well and sugar-free without the aid of insulin. Ten days before death he had fever and earache and vomited. At this time his urine was sugar-free. There was a blister on either auditory canal wall posteriorly near the tympanic membrane. The blisters were incised, and moist heat was applied externally. Relief was prompt. The vomiting ceased, and the temperature was normal the next day. The ears drained for several days but gradually dried. Two days before death the patient again became sick, vomited and had sugar in his urine. The blood sugar showed 422.5 mg. per one hundred cubic centimeters. Insulin, in 5 unit doses, was given every two hours. The next day the patient was restless and had a fever of 101 F. (38.3 C.). The ear canals were dry and the drums appeared normal. The reflexes were normal, except for the absence of knee jerks. Later in the day the fever increased and symptoms of meningeal irritation developed. Lumbar puncture revealed a slightly opaque fluid but no increased pressure. The patient died fifteen minutes later. The spinal fluid showed over 200 cells per cubic millimeter and a large number of long chain streptococci. The case is presented because of the rarity of the coexistence of these two diseases.

DISCUSSION

DR. J. W. ROSENFELD, Portland, Ore.: Was streptococcus meningitis the immediate cause of death?

DR. F. DOUGLAS, Seattle: Yes, we felt that death was due to streptococcus meningitis.

DR. A. REMBE, Seattle: Blisters on the tympanic membrane or in the ear canal near the membrane are a common occurrence and always bring up the point as to the advisability of opening them. Most of these blisters disappear without intervention.

DR. R. H. SOMERS, Seattle: My experience has been that these blisters are best let alone.

DR. C. L. SMITH, Seattle: This type of inflammation in the ear is usually an evidence of a subacute condition. In from 75 to 80 per cent of the cases all that is needed is an antiseptic, and the condition will subside without acute otitis media developing.

DR. F. DOUGLAS, Seattle: I feel that these blisters should be opened.

ON THE TREATMENT OF BURNS. DR. D. V. TRUEBLOOD, Seattle (by invitation).

The severity of a burn depends, first, on the amount of surface involved and, second, on the depth of the burn. Shock is the first thing to be considered. It is a mistake to treat the burn immediately. It may not be necessary even to take off the clothing. If clothing is adherent to the burn, one should cut around the area. Morphine is to be given for pain. Toxemia is to be considered next in importance. When a child dies from a burn, it is usually the result of toxemia. The problem is to reduce the amount of absorption; and this is best accomplished by the use of tannic acid either in the form of a bath (1 to 5 per cent solution) or spray. Tannic acid forms a crust or coagulum and thus retains body heat and moisture and makes the patient more comfortable. Mild burns are cured by tannic acid alone. One must also support the blood stream with blood transfusions, dextrose or salt solutions. If the child survives the shock and toxemia, one concentrates on the treatment of the wound itself. Melted paraffin applied directly to the wound by means of a spray or soft brush is the ideal treatment. If one suspects infection, a mild antiseptic like mercurochrome-220 soluble may be used. The chief advantages of paraffin are: 1. It tends to decrease the growth of granulating tissue. 2. It protects the islands of growing epithelium. 3. It is comfortable for the patient. 4. It retains heat and moisture. Splinting must be used to prevent contractures during healing.

DISCUSSION

DR. N. W. CLEIN, Seattle: If it becomes necessary to use skin grafts, should they be used early or late?

DR. A. S. MCCOWN, Seattle: Is the treatment of burns by the use of epinephrine hydrochloride in packs effective?

DR. S. G. HENRICKE, Portland, Ore.: Is the use of commercial preparations of tannic acid in jelly advisable?

DR. J. W. ROSENFELD, Portland, Ore.: Is it difficult to remove the paraffin, and how often should it be renewed?

DR. E. D. KANGA, Tacoma, Wash.: At what heat is the paraffin when applied? Patients are often relieved of the burning sensation by immersing the burned parts in water of a definite temperature for the first twelve to fourteen hours. The temperature of the water is not constant for different persons or for different kinds of burns.

DR. D. V. TRUEBLOOD, Seattle: The grafting stage is reached as soon as the wound is clean and before granulating tissue begins to form. It is not often that we have to use grafts. I am not familiar with the treatment with epinephrine hydrochloride. Tannic acid jelly seems to be satisfactory, but any ointment is difficult to remove. The tannic acid solution is much better. The paraffin should be removed every day. It is merely melted in an atomizer and held from one to one and one-half yards away from the wound and sprayed on. I have not used the water bath treatment.

DR. N. W. CLEIN, Seattle: What percentage of solution of tannic acid is used for a small burn, and how often is it applied?

DR. D. V. TRUEBLOOD, Seattle: I use a 1 to 5 per cent solution and apply it as often as is necessary until the brown crust is formed.

EPIDEMIC ENCEPHALITIS. DR. A. S. MCCOWN, Seattle.

An infant, aged 17 months, with a history of normal growth and development, seven weeks ago had a temperature of 101.2 F. (38.4 C.), vomited and had a convulsion. An injected pharynx was the only observation made on physical examination. The next day temperature was 103 F. (39.4 C.); the head rolled from side to side; the tongue protruded, and there was twitching of the extremities.

A puncture of the spine revealed a clear fluid without cell increase. Convulsive seizures continued at frequent intervals; the eyes turned to the left; there was twitching of the left arm and of the left side of the face. This would be followed in a few minutes by twitching of the right arm and of the leg. There was no ptosis and no opisthotonos. Repeated examinations of the spinal fluid were essentially negative. The eyegrounds were normal; the Mantoux test was negative. There were no convulsions after the first week, but at present, after seven weeks' illness, the patient is still unconscious, yet seems improved in that she reacts slightly to a bright light or a loud noise and turns over unaided.

DISCUSSION

DR. J. T. ABRAHAM, Wenatchee, Wash.: I had a similar condition in a child 8 years old who made a complete recovery after a hypertonic solution of dextrose was administered. Consciousness returned within five days.

DR. J. W. ROSENFELD, Portland, Ore.: Most patients tend to make a spontaneous recovery.

DR. A. H. SPOHN, Vancouver, B. C.: I had a case in a child, 3 years of age who had loss of voice and deafness for ten weeks but made an apparently complete recovery.

DR. J. B. BILDERBACK, Portland, Ore.: Do these children completely recover? They rarely return to normalcy. Most of them become mental problems.

DR. J. W. ROSENFELD, Portland, Ore.: I believe they make a spontaneous recovery from their acute illness regardless of the type of treatment.

DR. C. U. MOORE, Portland, Ore: It has been said that one third of the children die of epidemic encephalitis, one third recover without stigmas, and one third remain troublesome. In our cases one third made a complete recovery; there were not so many deaths, but there was a higher percentage of incorrigible children remaining. Our usual treatment is spinal taps; we also use a supportive treatment. The giving of 5 or 10 per cent dextrose solution subcutaneously is extremely important.

DR. J. I. DURAND, Seattle: Six or eight of the patients whom we recently treated were sick for only one week or ten days. The spinal fluid was under increased pressure. All the patients recovered promptly.

DR. N. W. CLEIN, Seattle: I have a case in a child, aged 2½ years, who has been unconscious for ten days. The patient is a neighbor of the patient in Dr. McCown's case. The spinal fluid is negative, and there is negative reaction to tests for tuberculosis. A high fever is present.

DR. R. H. SOMERS, Seattle: We must never forget the possibility of polioencephalitis; we must give convalescent serum before paralysis begins.

THE CARE OF CRANIOCEREBRAL INJURIES. DR. G. A. SWIFT, Seattle (by invitation).

The most important thing to consider immediately following an accident resulting in craniocerebral injury is treatment for shock. The symptoms of shock are rapid pulse and cold, sweaty skin. Fifty cubic centimeters of a 50 per cent solution of dextrose should be given intravenously. A roentgenogram should be taken only when the patient is well out of the state of shock. The patient cannot be saved if the brain has been badly traumatized. A glance at the chart with its half hour record of temperature, pulse and blood pressure will tell more than a glance at the patient. The pulse pressure should be compared with the pulse rate. When these two are the same one suspects edema or hemorrhage. For this secondary edema a spinal puncture or dehydration is the best treatment. Children usually respond quickly to dehydration. It is best produced by dextrose given intravenously two hours before magnesium sulphate is given by mouth. We rarely have to trephine. From five to seven days after recovery from shock one must be on the lookout for pneumonia.

DISCUSSION

DR. R. S. MILES, South Takoma, Wash.: Will Dr. Swift tell us what he thinks of the Frazier method of treatment, which, as I understand, consists of the early tapping of the spine, a dry diet and the limiting of fluids. The spine is tapped repeatedly, and the pressure measured.

DR. G. A. SWIFT, Seattle: Dr. Frazier now uses the same treatment as that of Dr. Fay. In medicolegal cases, spinal puncture should always be performed in order to determine the presence of free blood in the subarachnoid space. I limit the water intake to 20 ounces (0.6 Kg.) and permit the patient to receive only solid food.

A CASE OF IMPERFORATE ANUS. DR. H. E. COE, Seattle.

On this patient, a girl, aged 8 years, a left colostomy for an imperforate anus was performed when she was 3 days old. When 3 years old roentgenograms showed the sigmoid mobile but no downward stretch. The end of the sigmoid was 4 inches above the anus. A weight placed in the sigmoid and left for six months did not lessen the distance between the anus and the sigmoid. When 3 years and 8 months of age an exploratory laparotomy showed the bowel anchored at the colostomy. Weight was used three more months without improvement. At 4 years and 5 months of age, a right colostomy was done. This was unsatisfactory; four more operations were required to obtain satisfactory function. The last operation on the right colostomy was performed when the patient was 6 years and 4 months old with good results. At this time only mucus was coming from the left colostomy opening. Three months later a plastic operation was performed on the anal pit, which was deepened and lined with mucous membrane. At 7 years of age, the left colostomy was closed, and an end-to-end anastomosis done. Six months later, sigmoidopexy was performed, the tip of the sigmoid being fixed to the tip of the anal pit. Two weeks ago—the patient is now 8 years old—a two-stage operation was performed, the sigmoid being opened through the anal pit. There is now good sphincter action. Fecal discharge is slight. It is planned later to close the right colostomy opening.

EPITUBERCULOSIS IN A CHILD AGED EIGHT MONTHS, WITH A NEGATIVE MANTOUX TEST. DR. N. W. CLEIN, Seattle.

This patient, aged 8 months, has a negative family history and has been perfectly healthy and well all her life. She is well nourished and well developed. The roentgenograms of the chest revealed a fan-shaped shadow in the right upper side. Three skin tests for tuberculosis (Pirquet and Mantoux) have all been negative. If the shadow on the roentgenogram, which looks so typical, really shows epituberculosis, it is most unusual to find a negative Mantoux test.

DISCUSSION

DR. J. B. BILDERBACK, Portland, Ore. How can we be sure this is a case of tuberculosis?

DR. N. W. CLEIN, Seattle: I do not think we can say it is tuberculosis. We do not know what produces the shadow.

DR. S. G. HENRICKE, Portland, Ore: The shadow seen in epituberculosis is thought to be an allergic reaction. Is it not possible that we might have a similar allergic reaction from some other source?

DR. A. REMBE, Seattle: If this is a case of epituberculosis, the child should have a positive Mantoux test.

TREATMENT—SCIENTIFIC OR ADVERTISING. DR. N. W. CLEIN, Seattle.

Advertising relating to foods and drugs has become a menace to the medical profession. To safeguard its rights, the American Medical Association founded,

in 1905, the Council on Pharmacy and Chemistry and, in 1926, the Committee on Foods. Foods today occupy an equal place with drugs, biologic products and surgery in the control of human ailments. Most writers of advertisements for food and drug products have an exceedingly limited knowledge of foods, nutrition and drugs but an unlimited and versatile vocabulary and conscience as a guide in dramatizing the virtues of products they proclaim to the public.

In order to safeguard the rights of the medical profession as well as the right of the citizens of our communities to be informed accurately as to the scientific value of materials and foods, it is the duty of every doctor of medicine to carry the banner of truth. By prescribing misrepresented advertised products we give the public a false impression of unscientific preparations. (The speaker illustrated his point by displaying advertisements taken from popular magazines.) We should treat patients scientifically with the purpose of raising our own standards and dispelling the popular notion of the so-called value of advertised treatments.

DISCUSSION

DR. A. H. SPOHN, Vancouver, B. C.: It would be well if we looked into our own bathroom cupboards. The medical profession is also guilty. One of the difficult things to combat in the advertising of foods and drugs is that certain scientific facts are implied rather than stated.

DR. J. W. ROSENFELD, Portland, Ore.: What is Dr. Clein's formula for combating this abuse?

DR. N. L. THOMPSON, Everett, Wash.: A medical man should not apportion a certain amount of his overhead to advertising. This we do when we foster certain types of drugs and foods that are advertised for the general public. We are the people to say when and how much shall be given. The work of combating "self-treatment" should be done by the county medical societies in their local newspapers. Advertising should be improved, not by sporadic effort, but by continuity of effort.

DR. R. S. MILES, South Takoma, Wash: How are we going to get over this hump? I believe we should take the bull by the horns and see to it that the agents of these unethetical advertising concerns are kept out of our offices. We may get somewhere by discouraging these detail men.

DR. N. W. CLEIN, Seattle: There are a few firms that conduct good advertising. Each of us must do his part in every specific case.

DIPHTHERIA IMMUNIZATION: ITS METHODS AND RESULTS. DR. C. U. MOORE, Portland, Ore.

At birth 85 per cent of infants are immune to diphtheria because of a passive transfer of natural antitoxin through the placental blood. This passive immunity diminishes until, at the end of the first year, only 15 per cent of the patients are immune. Active immunization should be started at the age of 6 months so that the child may be protected at the period of greatest danger. Active immunization reduces the incidence of diphtheria in a ratio inversely proportional to the number immunized. Three doses of commercial toxin-antitoxin of 1 cc. each give immunity to from 53 to 90 per cent of those receiving it. Toxoid produces immunity in over 90 per cent of those receiving three doses totaling 2 cc. It has the further advantage over toxin-antitoxin of containing no horse serum and of being heat-stable. Antidiphtheritic ointment is valuable for its immunizing power, for use in allergic cases and for people who object to hypodermic injections. Up to 73 per cent are reported to become negative to the Schick test by this process. In our small series, toxin-antitoxin produced negative Schick tests in 53 per cent of one hundred and ten cases; toxoid, in 90 per cent of ten cases, and antidiphtheritic ointment in none of ten cases. This indicates the superiority of toxoid. To insure complete protection and to avoid bringing discredit on a valuable prophylactic measure, immunization should always be followed in from

four to six months by a Schick test. A repetition of the Schick test annually during the next two years precludes error and assures protection. It is now within the power of the medical profession to confer on humanity the blessing of universal immunity to diphtheria.

DISCUSSION

DR. H. L. MOON: As a routine I give two doses of 1 cc. of toxoid from two to three weeks apart. Lately I have been giving three doses.

DR. A. H. SPOHN, Vancouver, B. C.: Why use toxin-antitoxin at all when toxoid is so much better?

DR. W. F. PATRICK, Portland, Ore.: In older children and adults one should be careful about using toxoid because of the reaction that frequently occurs.

DR. A. H. SPOHN, Vancouver, B. C.: Is toxin-antitoxin preferable for adults? Is there any authority on this point?

DR. C. U. MOORE, Portland, Ore.: I myself have no experience giving either toxoid or toxin-antitoxin to adults. Park and others state that doses of 1 cc. of toxoid cause more severe reactions in adults and in older children than similar amounts of toxin-antitoxin. It is reported that the strength of supposedly standardized commercial products varies. In children of 12 years or over we have given 0.25 cc. of toxoid for the first dose, 0.5 cc. for the second and third doses and 0.75 cc. for the last dose. This may be excessive caution. At any rate, no unfavorable reactions have occurred. With increased experience we may give larger doses. The results of our postimmunization Schick tests make us feel that either a more uniformly potent product is desirable or a total of 3 cc. of toxoid should be given.

DR. A. H. SPOHN, Vancouver, B. C.: Toxoid is used almost entirely in Canada, where 0.5 cc., 0.5 cc. and 1 cc. are administered.

DR. N. W. CLEIN, Seattle: I have been giving two doses of 1.5 cc. at intervals of three weeks.

DR. A. H. SPOHN, Vancouver, B. C.: What is the determining factor between a positive and a negative reaction to the Schick test?

DR. C. U. MOORE, Portland, Ore: A reaction of 2 mm. or less in diameter on the seventh day is interpreted as negative, while a large red area or one that is 1 cm. in diameter or over is considered positive.

DR. J. W. ROSENFELD, Portland, Ore: How often should one look at the reaction to the Schick test?

DR. C. U. MOORE, Portland, Ore.: On the fourth and again on the seventh day.

THYMUS FREMITUS AS AN INDICATION FOR ROENTGENOTHERAPY. DR. A. E. WADE, Seattle.

Tactile fremitus elicited by the pressure of the finger-tip over the sternum is a valuable sign in differentiating those cases of stridor in infants which can be relieved by roentgenotherapy from those cases in which the stridor is not so satisfactorily relieved, whether the thymic shadow is enlarged or normal. This sign was present in 100 per cent of the cases of stridor in which relief was obtained by roentgenotherapy and absent in 100 per cent of the cases in which no relief was obtained by such therapy. The fremitus is best noted by lightly placing three or four finger-tips over the sternum during the presence of stridor. A vibration can be felt, and, as the fingers move to right and left, up and down, over the manubrial region, an outline can be forecast of the shadow later observed upon the roentgenograms. This sign has been dependable as an indication that roentgenotherapy will relieve the stridor, whether the anteroposterior shadow of the thymus is large or not. It reveals that there is density beneath the sternum sufficient to transmit the vibrations. All other causes of stridor are remote from

and not in contiguity with the thymus; hence they are not transmitted. Thirty cases of persistent stridor fall into four groups: (1) twelve infants, each with large anteroposterior thymic shadow, stridor and fremitus, relieved by roentgenotherapy; (2) four infants, each with normal thymic shadow but with stridor and thymic fremitus, relieved by roentgenotherapy; (3) four infants, each with large thymic shadow and stridor but no thymic fremitus, not relieved by roentgenotherapy although the thymus was reduced; (4) ten infants, each with stridor similar to thymic stridor with normal thymic shadow and no thymic fremitus, not given roentgenotherapy. In the last group, the condition of two was relieved by adenectomy, the condition of two others was diagnosed as laryngeal spasm incident to spasmophilia and relieved by calcium therapy, and in the other six no diagnosis was made, but all became normal in the course of four months. Perhaps the stridor was due to laxness of the laryngeal cartilages.

DISCUSSION

Dr. J. W. Rosenfeld, Portland, Ore.: Is fremitus as a single symptom sufficient to warrant roentgenotherapy? Stridor may be inspiratory or expiratory. Inspiratory stridors are usually due to defective arytenoid cartilages, while expiratory stridors may be due to the thymus. In a case in which there was an inspiratory and expiratory stridor roentgenotherapy was followed by improvement in the symptoms, but the patient died suddenly. I should like to ask if the relief from symptoms is permanent?

Dr. J. I. Durand, Seattle: During the last year I have not seen many enlarged thymuses. Dr. Jackson of Philadelphia has shown that the thymus can actually cause narrowing of the trachea.

Dr. F. R. Fischer, Spokane, Wash.: I saw a case in an infant in which the roentgenograms showed no enlargement of the thymus. Later the infant became ill with a mild infection of the upper respiratory tract and died suddenly. The thymus weighed 68 grains (4.4 Gm.). The depth of the thymus is most important, and one should not neglect to take a sagittal roentgenogram.

Dr. C. U. Moore, Portland, Ore.: Dr. Wade is to be congratulated on his new diagnostic idea. We find percussion so dependable that roentgenograms are ordered only in cases in which a transverse thymic dulness of 4 cm. or over occurs. Interns have little trouble learning to percuss a thymus accurately. Roentgen rays are expensive and may cause damage to the sensitive new-born child. Palpation and percussion methods are therefore preferable.

Dr. E. J. Barnett, Spokane, Wash.: Atropine will often give relief from stridor. Thymic hypertrophy and hypertonia may be related. Insufficient suprarenal secretion with resulting vagotonia may cause thymic hypertrophy. Atrophine and phenobarbital, U. S. P., will inhibit the stimulating effect of the vagus. Certain patients with exophthalmic goiter have been cured by receiving epinephrine by mouth.

Dr. A. H. Spohn, Vancoucer, B. C.: What happens in roentgenotherapy of the thymus? It is often difficult to find an illustration in a case of stridor. I know nothing about fremitus in enlarged thymus. It is difficult to interpret an enlarged thymus from the roentgenogram.

Dr. A. E. Wade, Seattle: Thymus fremitus is different from crying fremitus. One can get the fremitus only during the stridor. The vibration can be felt only with the finger-tips. One will not feel it with the flat of the hand.

Lipoid Nephrosis. Dr. H. H. Skinner, Yakima, Wash.

The patient, a child, aged 5 years, had general edema following severe sunburn and an infection of the upper respiratory tract. Chemical examination of the blood revealed: total protein, 6.93 mg.; albumin, 1.06 mg.; globulin, 4.3 mg., and fibrinogen, 1.57 mg. per hundred cubic centimeters. After one month of excessive

protein diet and therapy with thyroid extract (4 gr. [0.26 Gm.] daily), the edema completely disappeared. Albumin in the urine remained 4+ until four months of treatment; then it gradually diminished and in five months completely disappeared. The output of urine at the beginning of the fifth month was from 42 per cent to 45 per cent of the fluid intake. The percentage rose as the albumin disappeared from the urine. It had risen to 60 per cent by the third month and rose as high as 72 per cent when the urine became albumin-free. Later the child suffered from two acute infections; each time the urine showed some albumin, which quickly disappeared with the subsidence of the infection. The blood pressure varied from 90 systolic and 60 diastolic to 110 systolic and 70 diastolic.

PIGMENTED MOLE (MOVING PICTURE DEMONSTRATION). DR. H. H. SKINNER, Yakima, Wash.

At birth the patient presented a striking appearance, as so much of the skin surface was occupied by a pigmented mole. This was located chiefly on the posterior surface of the body. Sharply defined, its appearance resembled that of a cloak with a high curved collar thrown across the shoulders. The curve conformed to the edge of the occipital bone and extended a little forward on each side of the neck. It covered a small part of each side of the chest (anterior surface) and ran across the humerus at the same level, as if a line were drawn from the chest across the arms and around to the back. On either side of the thorax posteriorly, it extended nearly to the sacrum, although the areas were broken in the lumbar region. Between the scapulae the skin lay in thick but soft leathery folds. Isolated spots of varied sizes were on the limbs, soles and vulva; rather small spots occurred on the face. The infant otherwise appeared normal and developed well. But at the age of 6 weeks unmistakable signs of hydrocephalus were observed. The patient was moved away at this time and has not been studied since.

DISCUSSION

DR. N. W. MURPHY, Seattle: I have under observation a case of nephrosis with edema in which an attempt was made to produce dehydration with magnesium sulphate, but without success. Thyroid, 1 grain (0.65 Gm.), was given; then the dosage was increased to 11 grains (0.715 Gm.) daily, which increased the fluid output so that the patient lost 4 or 5 pounds (2 or 3 Kg.). Thyroid symptoms developed, and the dose was reduced to 7½ grains (0.488 Gm.) daily. The thyroid dosage was gradually reduced until none was given. At present there is no edema, but there is still albumin in the urine.

DR. H. T. CLAY, Tacoma, Wash.: Would it be possible to use the electric cautery on the small moles?

DR. C. U. MOORE, Portland, Ore: I am glad to know of the good results that Dr. Skinner has had. Our use of the high protein diet in this condition has been highly satisfactory. It seems logical that when a large amount of albumin is being lost in the urine the amount in the food should be augmented.

DR. A. H. SPOHN, Vancouver, B. C.: I had a case of marked edema; everything in the line of treatment had been tried, and the patient was apparently going to die. There was a marked amount of albumin in the urine. Thyroid therapy apparently cleared up the condition, and the patient has remained well for three years. I wonder if thyroid does not do some good in certain cases. In regard to the case of pigmented mole; I saw a case in which seventy-five large, raised, bluish nevi were removed successfully in a period of over nine months. Eight months later there was an enlarged spleen with marked anemia. Repeated transfusions were given. Masses developed in the abdomen, and the patient died. At autopsy the diagnosis was lymphosarcoma.

DR. J. I. DURAND, Seattle: In a case of nephrosis in a child with evidence of hyperthyroidism, the therapy with thyroid gland speeded up metabolism, bringing about gradual reduction of the edema. When the edema cleared up, signs of

hyperthyroidism developed. In treating nephritis or nephrosis one must give a balanced diet. We are not afraid of giving protein any more. One cannot improve the nephrosis at the expense of the child's nutrition.

Dr. W. F. Patrick, Portland, Ore.: In a case of a girl, aged 8 years, the distribution of nevi was worse than in the case presented by Dr. Skinner, as they were mostly on the face. Radium was used in treatment with some success. We must not forget the mental attitude toward nevi. The constant trying on the part of the parents to hide the deformity may have a marked effect on the child.

Dr. H. H. Skinner, Yakima, Wash.: In the case with nephrosis I believe the high protein diet helped the child more than the giving of thyroid. The clearing up of infection is necessary. From 80 to 85 per cent of the patients get well anyway; 5 per cent are benefited by medication, and 10 per cent die in spite of any kind of care. In the case of nevi the electric cautery can be used only on the small moles. Hemangiomas and moles belong to the class of nevi. It is important to treat the mental attitude of the child.

Book Reviews

Die Zuckerkrankheit und ihre Behandlung im Kindesalter. By Dr. Richard Priesel and Dr. Richard Wagner, Vienna. Price, 15.60 marks. Pp. 211, with 9 cuts. Leipzig: Georg Thieme, 1932.

This presentation offers a review of the latest studies in the principles of intermediary carbohydrate metabolism, correlated with a method of management of diabetes in children. The former is based on a comprehensive survey of the modern literature on the subject, and the latter on the authors' experience in the treatment of 130 diabetic children during the past nine years. The publication qualifies as a text in its field.

Certain phases of the book merit special comment. The authors believe that diabetes at any age is due basically to an inherited tendency, which is transmitted as a recessive characteristic. Their review of more than 1,000 reported cases seems to establish their contention. They develop the idea of the kinetics of sugar handling in a graphic manner. They believe that diabetes is dependent primarily on faulty glycogen fixation by the liver. It is pointed out that in early diabetes there is evidence of dysfunction rather than of mere hypofunction of the pancreas, and that spontaneous hypoglycemia may result at times.

The authors assume that the diabetic child should be treated as nearly like a normal child as his disease will permit. This requires adequacy of diet for normal growth and development and full activity. Under this premise, all children need insulin. Treatment is directed toward making the diet complete and attractive and supplementing the deficiency of pancreatic hormone with suitable doses of insulin. They base their dietary prescriptions on a modification of the Pirquet system of nutrition, with a calorie allowance of the basal needs plus from 75 to 100 per cent. This is somewhat lower than Pirquet recommends. From 10 to 15 per cent of the calories are furnished as protein, from 20 to 25 per cent as carbohydrate and the balance as fat. In desugarization and during coma they use starvation methods, and at times of reduced tolerance employ diets devoid of fat and animal protein, giving essentially cereal or vegetables. Five meals a day are scheduled, and the carbohydrate content of these is distributed to correspond to the time of the administration of insulin. The authors advocate two doses of insulin daily, at twelve hour intervals; in severe cases in which these are inadequate, they give three doses, at 6 a. m., 2:30 p. m. and 9:30 p. m.

A series of menus is presented, so designed that innumerable substitutions can be made without changing the available dextrose of the diet. To many students of child nutrition the choice of foods will seem rather unusual, and the menus do not present an optimum content of vitamins and minerals. Milk is used sparingly; vegetables and fruits receive less emphasis than is advantageous in the child's diet, and no mention is made of cod liver oil. In view of the fact that therapeutic diets are deficient so frequently unless special efforts are taken to forestall this and as the authors state that the diets are offered for the use of the practitioner who sees and treats but few children with diabetes, this criticism seems valid.

The patients that serve as a basis for the authors' conclusions grew and developed normally in every way, so far as could be determined. There was no evidence of lessened severity of the diabetes, however. It is their belief that progress of the disease is to be expected, parallel with, and in part dependent on, the growth of the child. The loss of tolerance through infections is emphasized. The question is raised as to the eugenic desirability of preserving these children, but the authors conclude that through the observation of the outcome of children treated with insulin, who approximate normality so closely, one may learn much in answering that and other questions concerning the condition.

Technischer Wegweiser für die Kinderpflege. By Dr. B. de Rudder. Price, 1.80 marks. Pp. 68. Berlin: Julius Springer, 1932.

This little textbook is primarily intended for nurses and other attendants. It specifically treats in considerable detail all the matters that enter into proper and adequate care of the well and the sick child. There are excellent common sense introductory comments about the general problem of child care and the elementary understanding of infant psychology.

The chapter on feeding and the commonly used artificial food mixtures is not too involved. The detailed directions for the preparation of the various mixtures are clear and easily understood.

Every conceivable therapeutic procedure is clearly discussed and so completely presented that it could be practically and effectively carried out by any person of even average intelligence.

The discussion of the care of the premature infant could have been more complete and is hardly adequate for so important a subject. The same is true of the discussion of the nursing care and treatment of acute pulmonary disorders, especially the various forms of pneumonia. In contrast to this, the various procedures of resuscitation are minutely and extensively described.

Excellent directions are given for nonsurgical diagnostic procedures, such as weighing, the taking of temperature, holding the infant for proper physical examination and catheterization.

The important technic of collecting specimens of urine is properly stressed, and directions are given for simple qualitative examination for albumin and sugar.

The directions for the various functional renal tests are excellent and are quite a unique feature of this little textbook.

The technic of the preparation for minor surgical procedures and proper assistance at such procedures is well described and is a feature generally missing in the average text of this kind.

In the final chapter, protection against infection from various contagious diseases is discussed, a subject that receives altogether too little attention in most of the textbooks written for nurses.

The style of the book is excellent. It fairly teems with good common sense direction and therapy.

Kinderpsychotherapie in der Praxis. By Dr. Curt Boenheim. With an introduction by Dr. Finkelstein. Price, 7.5 marks. Pp. 127. Berlin: Julius Springer, 1932.

The justification for the present volume is to be found in the preface: "This book is the result of the experience of ten years. My private practice and the cases seen in Finkelstein's Policlinic for children exhibiting neuroses or behavior problems have been the source of my material. . . . Continuous contact with clinical medicine, the use of all known diagnostic procedures and the observation of doubtful cases on the wards have been some of the factors which have supported my practical and scientific activities."

Boenheim's book shows the influence of these factors and hence may be recommended to all who wish to approach the functional disorders of childhood from the clinician's standpoint. It opens with a general discussion remarkable for the eclecticism with which he has extracted the kernels of rational observation from the various psychoanalytic and psychologic sects. In a space of thirty-one pages he has presented something that is more than a mere compilation of child psychology and psychotherapy, since it is illumined by clinical judgment and liberal empiricism.

The rest of the book deals with special problems: anorexia, vomiting, enuresis, masturbation, insomnia, tics, convulsions, etc. The author is frank to admit that symptomatic therapy in childhood is justifiable not only for practical reasons, but also because of the fundamental structure of the child's mind. The symptom is not necessarily an expression of deep character change. The naïvité of the child

has not permitted the construction of a psychologic system. The removal of the symptom may mean a radical cure. Boenheim appeals to every clinician when he advises conservatism in all therapy. Ruthless exploration in the "depths" of the child's mind bears the earmarks of a radical operation, which may have serious results. Boenheim is also loath to advise a change of environment as a routine procedure, since this merely avoids the issue; at some time the child must return to his home, and a relapse is inevitable. The only criticism that the reviewer can make is that Boenheim has perhaps underestimated the importance of early training as a cause for many of the behavior problems of the child.

Common Procedures in the Practice of Pediatrics. By Alan Brown, M.D., and Frederick F. Tisdall, M.D. Second edition. Pp. 300, with illustrations. Toronto: McClelland & Stewart, Ltd., 1932.

This is a revised and enlarged edition of the original book by the same authors. It is of eminently practical value to anybody dealing with children, not alone the pediatrician, but the general practitioner as well. Starting with history taking and physical examination, there are excellent chapters on infant feeding, acid-base metabolism, the preschool and the adolescent child and dietaries and various recipes, and also special diets for special conditions. Intelligence tests are described, as well as various diagnostic and therapeutic procedures. An entire chapter is devoted to a consideration of the parenteral administration of fluids, and one to special procedures, including the use and application of the oxygen tent and the treatment of various diseases. The giving of various preventive serums is also discussed. Another chapter is on difficulties in diagnosis and should prove especially interesting to the general practitioner. Finally, there is a short chapter on laboratory methods.

The whole book has a practical application, which is much to be commended.

La dentition chez les enfants. By Emile Cassonte. Price, 25 francs. Pp. 210. Paris: L'Expansion Scientifique Française, 1932.

This book is another of the "Bibliotheque de pathologie infantile" series, and continues the standard of former works in compactness and readability. It contains material on normal dentition, anomalies of late dentition, so-called symptoms, erosions, malformations, caries and infections. The discussions on physiology and diet are quite practicable. The English and American literature, as well as the French, has been well consulted.

Clinique médicale des enfants. Maladies infectieuses rhumatisme articulaire, aigu fiévre typhoide, scarlatine. By P. Nobécourt. Price, 55 francs. Pp. 420, with illustrations. Paris: Masson & Cie, 1932.

This is a collection of clinics on the three subjects named, namely, rheumatism, typhoid fever and scarlet fever. Each chapter takes up a special phase of the subject, citing in detail illustrative cases and commenting on the same. Each one of these chapters has been published previously in a medical magazine as a separate article, and they have all been combined in book form and placed in logical sequence. The book is a splendid example of the clinical side of the subjects as exemplified by one of the masters of French pediatrics.

Directory of Pediatric Societies

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor Taillens, Lausanne, Switzerland.
Secretary: Dr. P. Oltramare, rue Decandolle, Geneva, Switzerland.
Place: Geneva, Switzerland. Time: July 15, 1932.

International Pediatric Congress

President: Dr. George Frederic Still, 28 Queen Anne St., London, W. 1.
Place: London. Time: July 20-22, 1933.

FOREIGN

Royal Society of Medicine, Section for the Study of Disease in Children

President: Sir Henry Gauvain, 125 Harley St., W. 1, London.
Secretary: Dr. E. I. Lloyd, 33 Wimpole St., W. 1, London.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Frederic W. Schlutz, Bobs Roberts Hospital, University of Chicago, Chicago.
Secretary: Dr. Alfred A. Walker, Highland Plaza Apartments, Birmingham, Ala.
Place: Milwaukee. Time: 1933.

American Academy of Pediatrics

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.

American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st St., New York.

American Hospital Association, Section on Children's Hospitals

President: Dr. Thomas B. Cooley, 7815 E. Jefferson Ave., Detroit.
Secretary: Miss Bena M. Henderson, 721 N. 17th St., Milwaukee.
Place: Detroit. Time: September 12-16, 1932.

American Pediatric Society

President: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid, St. Louis.

Association of American Teachers of the Diseases of Children

President: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Secretary: Dr. Oscar Reiss, 1930 Wilshire Blvd., Los Angeles.

Canadian Society for the Study of Diseases of Children

President: Dr. G. A. Campbell, 164 Metcalfe St., Ottawa, Ontario.
Secretary-Treasurer: Dr. L. P. MacHaffie, 162 Clemow Ave., Ottawa, Ontario.
Place: Lucerne-in-Quebec. Time: June, 17-18, 1932.

SECTIONAL

Central States Pediatric Society

President: Dr. Frank C. Neff, 406 W. 34th St., Kansas City, Mo.
Secretary: Dr. A. H. Parmelee, 715 Lake St., Oak Park, Ill.
Place: Kansas City, Mo. Time: Fall, 1932.

North Pacific Pediatric Society

President: Dr. A. Howard Spohn, 925 West Georgia St., Vancouver, B. C.
Secretary: Dr. L. Howard Smith, 734 Medical Arts Bldg., Portland, Ore.

Southern Medical Association, Section on Pediatrics

Chairman: Dr. Horton Casparis, Vanderbilt University Hospital, Nashville, Tenn.
Secretary: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville, Fla.
Place: Birmingham, Ala. Time: November 16-18, 1932.

STATE

Alabama Pediatric Society

President: Dr. Thomas J. McElhenney, 1722, 2nd Ave., Bessemer.
Secretary-Treasurer: Dr. John W. Simpson, 1117 S. 22d St., Birmingham.

Georgia Pediatric Society

President: Dr. Charles E. Boynton, 118 Forrest Ave., N. E., Atlanta.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.

Louisiana State Pediatric Society

President: Dr. R. T. Lucas, Shreveport, La.
Secretary-Treasurer: Dr. Suzanne Schaeffer, Chailie Bldg., New Orleans.

Medical Society of State of New York

Chairman: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester.
Secretary: Dr. Adolph G. G. De Sanctis, 12 E. 11th St., New York.

Nebraska Pediatric Society

President: Dr. H. B. Hamilton, 434 Aquila Court Bldg., Omaha.
Secretary: Dr. George L. Clark, 1817 Vinton St., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive, 6 p. m.

North Carolina Pediatric Society

President: Dr. Yates W. Faison, 121 W. 7th St., Charlotte.
Secretary: Dr. E. K. McLean, 121 W. 7th St., Charlotte.
Place: Various children's hospitals. Time: Twice a year.

Oklahoma State Pediatric Society

President: Dr. C. E. Bradley, Medical Arts Bldg., Tulsa.
Secretary: Dr. G. H. Harrison, 1200 N. Walker St., Oklahoma City.

South Carolina Pediatric Society

President: Dr. T. D. Dotterer, 1512 Marion, Columbia.
Secretary-Treasurer: Dr. Julian P. Price, 117 W. Cheves St., Florence.

Texas Pediatric Society

President: Dr. J. H. Park, Jr., 3717 Main St., Houston.
Secretary-Treasurer: Dr. P. E. Luecke, 4105 Live Oak St., Dallas.

Virginia Pediatric Society

President: Dr. St. Geo. Grinnan, 925 W. Grace St., Richmond.
Secretary-Treasurer: Dr. J. B. Stone, 2042 Park Ave., Richmond.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. E. McClelland, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. P. G. Albrecht, 2009 Adelbert Rd., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

Academy of Medicine, Toronto, Section of Pediatrics

Secretary: Dr. Lawrence Murray, 1870 Bloor St., W., Toronto.
President: Dr. Gladys Boyd, 56 DeLisle St., Toronto.

Bronx Pediatric Society

President: Dr. Joseph Golomb, 496 E. 17th St., New York.
Secretary: Dr. E. Leonard Benjamin, 2229 Valentine Ave., New York.
Place: Concourse Plaza, 161st St. and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

Brooklyn Pediatric Society

President: Dr. Irwin Schiff, 658 Eastern Parkway, Brooklyn.
Secretary: Dr. Louis A. Koch, 62 Pierrepont St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

Chicago Pediatric Society

President: Dr. Henry E. Irish, 432 S. Lincoln St., Chicago.
Secretary: Dr. Bert I. Beverly, 8 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

Dallas County Pediatric Society

President: Dr. Gordon B. McFarland, Medical Arts Bldg., Dallas, Texas.
Secretary: Dr. Harold T. Nesbit, Medical Arts Bldg., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

Detroit Pediatric Society

President: Dr. Charles Wilson, 10 Peterboro St., Detroit.
Secretary: Dr. Joseph A. Johnston, Henry Ford Hospital, Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: T. Bolling Gay, 384 Peachtree St., Atlanta.
Secretary: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Place: Academy of Medicine, 32 Howard St. Time: Second Thursday of each month from October to April, 8 p. m.

Memphis Pediatric Society

President: Dr. William R. Graves, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry J. Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

Milwaukee Pediatric Society

President: Dr. G. H. Fellman, 231 W. Wisconsin Ave., Milwaukee.
Secretary: Dr. George F. Kelly, 161 W. Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. Lewis Webb Hill, 319 Longwood Ave., Boston.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Herbert B. Wilcox, 39 E. 75th St., New York.
Secretary: Dr. John Caffey, 50 Haven Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northern California Pediatric Society

President: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Secretary-Treasurer: Dr. Lloyd Hardgrave, 384 Post St., San Francisco.
Place: Various teaching schools. Time: Monthly.

Northwestern Pediatric Society

President: Dr. Samuel Amberg, Mayo Clinic, Rochester, Minn.
Secretary: Dr. Alexander Stewart, 459 Lowry Medical Arts Bldg., St. Paul.

Philadelhia Pediatric Society

President: Dr. John P. Scott, 2040 Pine St., Philadelphia.
Secretary: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala-Cynwyd, Pa.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. David H. Boyd, 200, 9th St., Pittsburgh.
Secretary: Dr. Theodore O. Elterich, 724 Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. John S. Weitzel, 3103 W. Franklin St., Richmond, Va.
Secretary-Treasurer: Dr. W. E. Chapin, 922 Floyd Ave., Richmond, Va.
Place: Retreat for the Sick, 2621 Grove Ave. Time: First Thursday of each month (other than during the summer).

Rochester Pediatric Society

President: Dr. S. W. Clausen, Strong Memorial Hospital, Rochester, N. Y.
Secretary: Dr. F. W. Bush, 221 S. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: First Friday of each month from October to May.

Rocky Mountain Pediatric Society

President: Dr. C. H. Platz, Fort Collins, Colo.
Secretary: Dr. R. H. Verploeg, 1850 Gilpin St., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month from September to May, inclusive, 2:30 p. m.

St. Louis Pediatric Society

President: Dr. Gustave Lippmann, 3720 Washington Blvd., St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, 3720 Washington Blvd., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. C. L. Smith, 1215, 4th Ave., Seattle.
Secretary: Dr. N. W. Murphy, 515 Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

Southwestern Pediatric Society

President: Dr. Donald K. Woods, 2545 4th Ave., San Diego, Calif.
Secretary: Dr. Jeanette Harrison, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Henry G. Poncher, 5325 Kenmore Ave., Chicago.
Secretary: Dr. John P. Parsons, 320 S. Division St., Ann Arbor, Mich.
Place: Ann Arbor, Mich. Time: November, 1932.

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